TABLE 3-10

Sources and Estimated Atmospheric Emissions of Manganese in 1968[a]

Product/Process	Particulate Emissions (kg/mt product)	Particulate Mn Content (%)	Average or Predominant Particle Size (μm)	Control Efficiency or Prevalence of Use (%)	Mn Emission Factor (kg/mt product)	1968 Volume (10^3 mt product)	Estimated 1968 Emissions (mt)	Percent of Total Emissions
Mn metal/ electrolytic	NA	NA	NA	NA	2.5	24	295	1.7
Ferromanganese/ blast furnace	205	15-25	0.3	95	2.1	481	1010	5.9
Ferromanganese/ electric furnace	NA	20-25 (33% Mn Oxide)	<2	NA	12	273	3330	19.3
Silicomanganese/ electric furnace	NA	NA	NA	NA	35	109	3780	21.9
Pig iron/blast furnace	75	0.5	NA	97	0.011	80,700	910	5.3
Steel/open hearth furnace	4-10.5	0.5	0.5	40	0.026	59,000	1506	8.7
Steel/basic oxygen furnace	23	3.2 (4.4% Mn_3O_4)	0.5-1.0	97	0.022	43,500	962	5.6
Steel/electric furnace	5.5-5.5	3.1 (4% MnO)	<5	78	0.039	14,500	562	3.2
Cast iron/cupola furnace	11	2	NA	25	0.165	15,200	2510	14.5
Welding rods	NA	NA	NA	NA	8[b]	2.7[b]	21.8	0.1
Nonferrous alloys	NA	NA	NA	NA	6[b]	9.1[b]	54.4	0.3
Batteries	NA	NA	NA	NA	5[b]	16.3[b]	81.6	0.5
Chemicals and miscellaneous	NA	NA	NA	NA	5[b]	54[b]	270	1.6
Mining	NA	NA	NA	NA	0.1[b]	43.5[b]	4.4	0.03
Coal combustion	40-70	0.02-0.03	NA	75	0.0042	462,000	1950	11.3
Residual fuel oil	NA	NA	NA	10	NA	669x10^6 bbl	6.4	3.04

[a]Source: Adapted from U.S. EPA, 1971

[b]On a basis of tons manganese, not tons product

NA = Not available

major emission source, has declined substantially; combined 1981 production was ~31% of 1968 production, and 1982 production estimates showed substantial further declines (see Table 3-7). Process emissions of manganese may also be much lower than those indicated in 1968. Blast furnaces, reportedly the most prolific polluter of any metallurgical process when not controlled (Wurts, 1959), have not been used since 1977 (Matricardi and Downing, 1981). In addition, more recent measurements indicate lower emission factors for controlled submerged-arc facilities (Table 3-11). Ambient air measurements in the vicinity of ferromanganese manufacturing indicate that recent manganese levels were lower by about an order of magnitude than those recorded during the mid-1960s (see Section 3.6.1.2.).

3.4.2.2. IRON AND STEEL MANUFACTURE -- There is considerable loss of manganese in iron and steel production. Manganese is lost to fume, slag or other waste products at each stage of production; however, the most significant loss is to fume and slag in the furnace. Particulates from the furnace tend to be submicron in size. Table 3-10 indicates that particulate manganese content (<5%) is less than for ferromanganese manufacture, but total emissions are comparable because of the larger production volume. Other sources (U.S. EPA, 1981a) have listed a higher manganese content (9.7%) for aerosol from a steel electric furnace (see Section 3.4.3.). Manganese emissions in 1968 were estimated at ~6500 mt, or ~37% of total U.S. emissions (see Table 3-10). Production levels have decreased somewhat; pig iron production in 1980 was 78% of 1968 levels, and 1980 steel production was 85% of 1968 levels (DeHuff, 1961-1980; DeHuff and Jones, 1981).

3.4.2.3. FOSSIL FUEL COMBUSTION -- Manganese is emitted to the atmosphere by the burning of coal and other fuels containing natural trace levels of manganese. The use of manganese fuel additives constitutes an

TABLE 3-11

Estimated Manganese Emissions from Controlled Submerged-Arc Furnaces Producing Manganese Alloys

Furnace Type	Product	Control Type	Control Efficiency (%)	Particulate Emission Factor (kg/mt product)	Manganese Emission Factor[a] (kg Mn/mt product)	Reference
Open	silicomanganese	scrubber	99.1	0.73	0.15	U.S. EPA, 1971
Open	silicomanganese	scrubber	94.0[b]	3.25	0.65	U.S. EPA, 1971
Open	high carbon ferromanganese	scrubber	[illegible]	0.79	0.16	U.S. EPA, 1981b
Semi-sealed	silicomanganese	scrubber	>99.1[b]	0.05	0.010	U.S. EPA, 1971
Semi-sealed	high carbon ferromanganese	scrubber	>99.1[b]	0.03	0.015	U.S. EPA, 1971
Semi-sealed	high carbon ferromanganese	scrubber	98[b]	0.16	0.08	U.S. EPA, 1981b
Totally sealed	silicomanganese	scrubber	NA	0.062	0.012	U.S. EPA, 1979b

[a]Assumes manganese content of particulate is 20%.

[b]Does not include losses during tapping of the metal.

additional source. The average and range for manganese concentration in various fuels and preparations are shown in Table 3-12. The range of manganese content in coal ash is presented in Table 3-13.

Coal combustion was estimated to be the source of ~11% of total manganese emissions in 1968 (see Table 3-10). The emission factor assumed an average manganese content of 26.4 µg/g in coal, and penetration to the atmosphere of ~16% (U.S. EPA, 1971). U.S. consumption of coal in 1980 was 640.4×10^6 mt, an increase of ~39% over 1968 (Energy Information Administration, 1980). However, recent measurements from coal-fired power plants equipped with electrostatic precipitators (ESPs) showed manganese penetrations of 0.07-0.13% for one plant, and 1.6% for another plant with partial ESP malfunction (Ondov et al., 1979). Estimates of average penetrations for the range of plants currently operating are not available.

While collection efficiencies may be high, some evidence indicates that metal concentrations are higher in the smaller-diameter particles which are less efficiently collected. Analyses of size-fractioned fly-ash collected from a coal-fired power plant precipitator showed that manganese concentrations were highest (1090-1180 µg/g) in particles of 0.2-1.5 µm, whereas concentrations of 500-800 µg/g were found among particles of 3 to >140 µm (Smith et al., 1979). A similar trend but with lower concentrations (150-470 µg/g, increasing as particle size decreases) was found in airborne material not retained by a cyclonic precipitator in another coal-fired power plant (Davison et al., 1974). The elemental mass median diameter for manganese for the two ESP-equipped plants described above was ~2.3 µm for the more-efficient and ~8.2 µm for the less-efficient ESP (Ondov et al., 1979).

TABLE 3-12

Manganese Concentrations of Coal, Fuel Oil, Crude Oil, Gasoline, Fuel Additives and Motor Oil*

Sample	Number of Samples	Average Concentration	Range
Coal	76	37 µg/g	5-80 µg/g
Residual fuel oil	20	0.136 µg/g	0.012-0.27 µg/g
Crude oil	20	0.031 µg/g	<0.001-0.15 µg/g
Regular gasoline			
Brand A	10	<0.005 µg/mℓ	<0.001-0.01 µg/mℓ
Brand B	9	<0.0066 µg/mℓ	<0.001-0.01 µg/mℓ
Premium gasoline			
Brand A	10	0.0144 µg/mℓ	0.002-0.02 µg/mℓ
Brand B	8	0.0052 µg/mℓ	0.002-0.02 µg/mℓ
Fuel additives			
Gas treatment	3	0.038 µg/mℓ	0.019-0.042 µg/mℓ
Fuel-mix tune up	3	<0.5 µg/mℓ	<0.5 µg/mℓ
Engine tune up	3	<0.003 µg/mℓ	<0.003 µg/mℓ
Gas power booster	3	0.009 µg/mℓ	0.008-0.010 µg/mℓ
Gas treatment	3	0.012 µg/mℓ	0.016-0.019 µg/mℓ
Gasoline antifreeze	3	0.007 µg/mℓ	0.006-0.009 µg/mℓ
Gas booster	6	0.051 µg/mℓ	0.008-0.096 µg/mℓ
Carburetor tune up	3	-	0.272-2.71 µg/mℓ
Motor oil	4	0.023 µg/mℓ	0.004-0.08 µg/mℓ

*Source: U.S. EPA, 1975, based on reports of Ruch et al., 1973 and Jungers, 1973

TABLE 3-13

Manganese Content in Coal Ash*

Type of Coal	Range of Content (mg/g)
Pennsylvania Anthracite	0.05-0.9
Texas, Colorado, North and South Dakota	0.1 -10
West Virginia	0.12-1.8
Montana	3.3
Alabama	0.4-0.5

*Source: Abernathy et al., 1969

The manganese content of petroleum is lower by >2 orders of magnitude than that of coal (see Table 3-12). Therefore, regardless of changes in residual fuel oil combustion and emission control practices, oil combustion constitutes a minor source of ambient manganese.

Piver (1974) reported that MMT production prior to its use in unleaded fuel was ~500 tons/year, or ~125 tons as manganese. Ethyl Corporation reported that during peak use of MMT prior to the ban in 1978, consumption was ~3750 tons/year, or ~940 tons as manganese (Hall, 1983b). Estimates of the percentage of manganese emitted from the tailpipe range from 15-30% of the amount burned (Ethyl Corporation, 1972; Pierson et al, 1978), resulting in an estimate of 140-280 tons of manganese emitted per year during the peak of MMT use. The emitted manganese has been described as consisting primarily of Mn_3O_4, in particles of 0.30-0.38 μm mass median diameter (Ethyl Corporation, 1972). However, the emission of water-soluble forms from catalyst-equipped vehicles capable of producing H_2SO_4 cannot be ruled out (Pierson et al., 1978). The manganese content of particulate from two automobiles burning gasoline containing MMT (at 0.125 g/gal) ranged from 1.4-3.1%, and averaged 3.0% (Ethyl Corporation, 1973). Current use of MMT at ~0.05 g Mn/gal in ~20% of leaded gasoline (Hall, 1983) results in a substantially lower emissions estimate than that given for 1977.

Estimates have been made of ambient air concentrations of manganese which could result from specified levels of MMT usage. These estimates are based on analogy to lead, for which both fuel concentrations and resulting ambient concentrations are known. Accordingly, 100% usage of MMT at 0.125 g Mn/gal would be estimated to result in ambient manganese concentrations ranging from 0-0.25 $\mu g/m^3$, with a mean urban value of 0.05 $\mu g/m^3$, in addition to already existing concentrations (Ter Haar et al., 1975) (see Section 3.6.1. for data on existing ambient manganese concentrations).

Additional manganese concentrations of 0.16 $\mu g/m^3$ as an average and up to 0.52 $\mu g/m^3$ near freeways would be estimated for Southern California (Hidy et al., 1977). Usage levels lower than 0.125 g Mn/gal would result in proportionally lower estimates for ambient air.

Actual vehicle emissions of manganese were calculated by sampling air in tunnels of the Pennsylvania turnpike during 1975-1977 (Pierson et al., 1978). Calculations include the total vehicle-generated aerosol, not simply exhaust. Manganese content of fuel at uproad turnpike service plazas was also monitored. Manganese emission rates for gasoline-powered vehicles were 0.03-0.05 mg Mn/km during 1975-1976 while MMT use was minimal (1-4 mg Mn/gal). By 1977 MMT use was more frequent, giving an average for all gasoline sampled of 16 mg Mn/gal, and the emission rate was 0.08 mg Mn/km. However, manganese concentrations in the tunnel air, which averaged 0.11 $\mu g/m^3$, showed no trend over the period of study. The reason for this lack of an overall increase was that manganese emissions for diesel trucks were large (0.32-0.69 mg Mn/km) and overshadowed the change resulting from MMT. Part of the manganese in diesel emissions originated from road dust, but the source of the remainder was unknown, as only traces of manganese were present in the diesel fuel (Pierson et al., 1978).

3.4.3. Relative Importance of Manganese Sources at Several Locations as Determined by Mass Balance and Enrichment Models. The availability of increasingly sensitive analytical techniques for determining the elemental composition of ambient airborne particulate matter has enabled the use of statistical methods to identify the most likely emission sources. Elemental composition patterns for ambient particulates at a "receptor" or monitoring site can be compared with known or statistically constructed composition patterns for particles from a number of sources. Using chemical mass

balance techniques, the total ambient aerosol mass and the mass of each element at the receptor can then be apportioned among the sources (Cooper and Watson, 1980; Alpert and Hopke, 1981; U.S. EPA, 1981a). The separation of coarse (e.g., >2.5 μm) and fine particle fractions by a dichotomous sampler can result in better resolution of sources (Dzubay, 1980; Alpert and Hopke, 1981). Many applications of source apportionment techniques have included data on manganese.

In the Portland Aerosol Characterization Study, a priori determination was made of the elemental composition of aerosols from several sources (Table 3-14) (Cooper and Watson, 1980; U.S. EPA, 1981a). The manganese component varied from 173 mg/g (17.3%), for ferromanganese furnace emissions, to "0 mg/g", for leaded automobile exhaust. The elemental compositions for several sources (soil, road dust, asphalt production, rock crusher and coal fly ash) were so similar that they could not readily be distinguished; the manganese concentration of these aerosols varied only from 0.3-2 mg/g (Cooper and Watson, 1980).

Dzubay (1980) used six source terms for apportioning Regional Air Pollution Study (RAPS) data from dichotomous samplers in St. Louis, Missouri. Some of the terms used were composites, representing several natural and anthropogenic processes which could not be distinguished. The crustal-shale component included soil or dust suspended by wind or human activities (e.g., vehicle traffic, earth-moving, argriculture, etc.), particulates from quarrying or other manufacturing processes, and/or fly ash. The crustal-limestone component included suspended calcium-rich soil, cement dust from vehicles or cement manufacture, and/or other manufacturing processes. The term for steel industry emissions might also have included natural or anthropogenic suspension of iron-rich soil. The elemental compositions for

TABLE 3-14

Manganese Concentration in Fine (<2.0 μm) and Coarse (2.0-20 μm) Particle Fractions of Aerosols from Several Sources in the Portland Aerosol Characterization Study*

Aerosol Source	Mn Concentration (mg/g)	
	Fine Particles	Coarse Particles
Marine	NR	0.0
Soil	2.0	0.85
Road dust	1.23	1.0
Leaded auto exhaust	0.0	0.0
Residual oil combustion	0.46	0.46
Distillate oil	0.14	NR
Vegetative Burn 1	1.2	1.2
Vegetative Burn 2	0.47	0.47
Kraft recovery boiler	0.3	5.2
Sulfite recovery boiler	0.54	0.54
Hog fuel boiler	5.1	2.9
Aluminum processing	0.11	0.0
Steel electric furnace	87	87
Ferromanganese furnace	173	173
Carborundum	0.35	0.29
Glass furnace	0.021	0.031
Carbide furnace	0.42	0.36
Asphalt production	2.0	NR
Rock crusher	0.8	NR
Coal fly ash	0.3	NR

*Source: U.S. EPA, 1981a; Cooper and Watson, 1980

NR = Not reported

source aerosols were assigned a priori, based on data from various studies. The manganese component of each source, and the estimated contribution of each source to ambient manganese and total aerosol mass are given for the coarse particle fraction at one St. Louis receptor site (site 106) for August and September, 1976 (Table 3-15). Dzubay et al. (1981) used similar source terms in an analysis of data for January, 1979, from a single dichotomous sampler in Denver, Colorado. These source apportionment data for both fine and coarse particle fractions are also shown in Table 3-15. A comparison of coarse particle sources for the St. Louis and Denver sites shows that the proportion of manganese contributed by the crustal-shale source was much greater in Denver, in the absence of the paint pigment and steel sources found in St. Louis. Comparison of fine and coarse fractions in Denver shows that while crustal-shale was the predominant source of manganese in coarse particles, vehicle exhaust evidently was the main manganese source in fine particles.

Hopke and coworkers (Alpert and Hopke, 1981; Liu et al., 1982) applied target transformation factor analysis (TTFA) to other subsets of the St. Louis RAPS data. In TTFA, source aerosol composition is determined through both a priori knowledge of source characteristics and a posteriori selection and adjustment based on factor analysis and chemical element balance techniques applied to the receptor data set. These source refinement methods were applied individually to fine and coarse data sets at RAPS site 112 for July and August, 1976 (Table 3-16, part A), and to all 10 St. Louis RAPS sites during a single week beginning July 31, 1976 (Table 3-16, part B) (Alpert and Hopke, 1981).

TABLE 3-15

Manganese Concentration in Aerosols from Various Sources, and Estimated Percent Contribution of Each Source to Observed Ambient Manganese and Total Aerosol Mass at Two Sites

Source	Mn in Source Aerosol (mg/g)	St. Louis, MO RAPS Site 106[a]		Denver, CO Site[b]	
		Contribution to Ambient Aerosol Mass (%)[c]	Contribution to Ambient Mn (%)[c]	Contribution to Ambient Aerosol Mass (%)[c]	Contribution to Ambient Mn (%)[c]
FINE PARTICLES[d]					
Ammonium sulfate	0.0	NR	NR	15.8	0
Motor vehicle exhaust	0.6	NR	NR	25.3	80
Crustal-shale[e]	0.85	NR	NR	2.2	20
Crustal-limestone[e]	1.1	NR	NR	0.5	0
Road salt	0.0	NI	NI	1.1	0
Refuse incineration	0.7	NI	NI	0.2	0
COARSE PARTICLES[d]					
Ammonium sulfate	0.0	7.1	0.0	0.4	0
Motor vehicle exhaust	0.6	4.5	2.9	7.3	5.6
Crustal-shale[e]	0.85	51.5	34.3	54.0	66.7
Crustal-limestone[e]	1.1	29.4	25.7	2.5	5.6
Paint pigment	4.0	3.4	8.6	NI	NI
Steel[e]	31.0	1.9	48.6	NI	NI
Road salt	0.0	NI	NI	10.9	0
Refuse incineration	0.7	NI	NI	0.6	0

[a]Derived from Ozubay, 1980

[b]Derived from Ozubay et al., 1981

[c]Percentages may not sum to 100% when model under- or overestimates Mn concentration or aerosol mass.

[d]St. Louis study: fine <2.4 μm, coarse 2.4-20 μm. Denver study: fine <2.5 μm, coarse 2.5-15 μm

[e]Composite of natural and anthropogenic sources; see text

NI = Not included in analysis for this site; NR = not reported

TABLE 3-16

Manganese Concentration in Aerosols from Various Sources, and Estimated Percent Contribution of Each Source to Observed Ambient Mn and Total Aerosol Mass, Based on Target Transformation Factor Analysis.[a]

Source	Mn in Source Aerosol (mg/g)	Contribution to Ambient Aerosol Mass (%)	Contribution to Ambient Mn (%)[b]
A. RAPS Site 112, St. Louis, MO, July and August, 1976			
FINE FRACTION (<2.4 μm)			
Motor vehicle	0.0	15	0.0
Sulfate	0.0	65	0.0
Fly ash/Soil	0.7	11	13.5
Paint	4.8	1	11.8
Refuse incineration	8.6	4	64.7
Unknown	NR	4	NR
COARSE FRACTION (2.4-20 μm)			
Soil	0.8	54	38.5
Limestone	1.6	27	38.5
Sulfate	1.0	12	10.3
Paint	1.2	7	7.7
B. 10 RAPS Sites, St. Louis, MO, Week of July 31, 1976			
FINE FRACTION (<2.4 μm)			
Sulfate	0.0	84	0.0
Steel	7.1	7	83.3
Motor vehicle	0.7	6	6.7
Zinc/Lead smelter	0.8	2	4.2
Unknown	NR	1	NR

TABLE 3-16 (cont.)

Source	Mn in Source Aerosol (mg/g)	Contribution to Ambient Aerosol Mass (%)	Contribution to Ambient Mn (%)[b]
COARSE FRACTION (2.4-20 μm)			
Soil	1.1	31	21.7
Steel	23.0	5	75.0
Limestone	0.0	39	0.0
Sulfate	1.7	11	11.3
Soil/Fly ash	0.0	10	0.0
Unknown	NR	4	NR

[a]Derived from Alpert and Hopke, 1981

[b]Percentages do not sum to 100% because model slightly under- or overestimated Mn concentration.

NR = Not reported

A direct comparison of the TTFA results with those of Dzubay (1980) for St. Louis is not possible since the same data sets were not used. The studies evidently detected differences in aerosol sources among the sites. Site 106 (see Table 3-15) and several of the other sites (Table 3-16, part B) are located in close proximity to iron works and foundries, whereas site 112 (Table 3-16, part A) is not. These differences are reflected in the absence of a resolvable steel source at the latter site. However, the refinement of sources by TTFA results in certain irregularities where a minor element such as manganese is concerned. The attribution of coarse-fraction manganese to a sulfate source term (Table 16) was acknowledged by the authors to be irregular. This result may be a sampling artifact (i.e., due to condensation of SO_2 on coarse Mn-containing particles) or may result from "source lumping" due to an inability to resolve other minor, manganese-containing sources. The absence of manganese from the limestone and soil/fly ash source terms (Table 3-16, part B) is also rather implausible, and further indicates the deficiencies of this technique.

In source apportionment studies of particulates in New York City, manganese was used as a tracer for suspended dust and soils (Kleinman et al., 1980; Kneip et al., 1983). Regression models were used to derive coefficients relating tracer mass in ambient air to mass of particulates from the traced source. Other sources which also undoubtedly contributed to airborne manganese, such as vehicle emissions, fuel oil burning, and incineration, were traced by other elements. Since the manganese concentration in dust and soil probably is relatively stable, changes in the manganese coefficient over time are probably related (inversely) to changes in relative contributions from nonsoil-related sources. From the period 1972-1973 to the period 1977-1979, the manganese coefficient ($\pm$ S.E.) for total suspended particu-

late (TSP) increased from 420±200 to 840±311, indicating a substantial reduction of manganese emissions from nonsoil sources. These changes would be expected due to the elimination of MMT usage in unleaded gasoline and reduction of incineration during this period (Kleinman et al., 1980; Kneip et al., 1983). A concommitant reduction in mean TSP from 82±2 to 54±2 $\mu g/m^3$ was seen during this period. However, during the period 1979-1980, a decrease in the manganese coefficient to 670±160 seemed to indicate increasing nonsoil contributions, and was accompanied by an increase in mean TSP to 66±2 $\mu g/m^3$ (Kneip et al., 1983).

A simpler method for making inferences about particulate sources from receptor data is by the use of an enrichment factor (EF) model. The ratio of the concentration of the element in question to that of a reference element is compared for an ambient aerosol and a background aerosol or source material, to determine whether the element is enriched with respect to the reference element (Cooper and Watson, 1980). The crustal contribution of manganese to ambient aerosols has been evaluated using aluminum as a crustal reference element, as follows:

$$\text{Crustal EF} = \frac{(\text{Mn/Al})_{\text{air}}}{(\text{Mn/Al})_{\text{crust}}}$$

Values for elements arising exclusively from crustal material should be near unity, although some variation would be expected due to natural variations in soil (see Section 3.4.1.). As mentioned previously, crustal material suspended by natural processes is indistinguishable by these methods from crustal material suspended by human activities. However, values of crustal EF for elements such as lead, which are highly enriched from noncrustal sources, may be as high as 10^4 (Bernstein and Rahn, 1979; Lewis and Macias, 1980).

Duce et al. (1974) reported a crustal EF of 2.6 for manganese over the Atlantic Ocean north of 30°N. Bernstein and Rahn (1979) reported the elemental composition of fine (<2.5 μm) and total aerosol from New York City for August, 1976. They derived a crustal EF for manganese of 4.6, and also reported EF values of 5.7, 0.56 and 0.54 for Philadelphia, Bermuda and Tucson, respectively. Although the latter two values were lower by a factor of 10, manganese was not considered to be enriched in the New York aerosol. However, these EF values were based on total aerosol analyses. Calculation of EF for the fine particle fraction alone gives a value of ≈4.3, or ≈3 times higher.

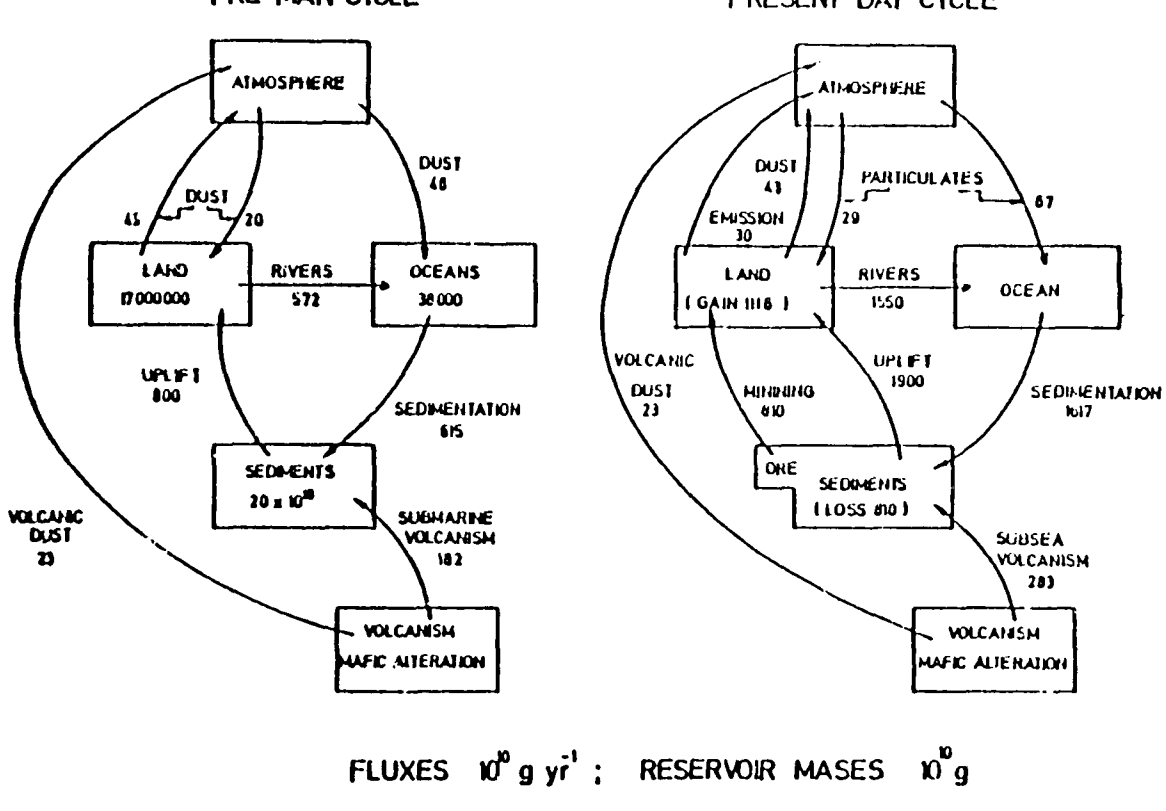
Bernstein and Rahn (1979) used a crustal Mn:Al ratio of 0.011 to calculate crustal EF for manganese. Very similar ratios are found by examining the "crustal-shale" composition data used by Dzubay (1980) and Dzubay et al. (1981), and the soil, road dust and rock-crusher aerosol composition data reported by Cooper and Watson (1980). Using this ratio as a crustal reference, the EF model was applied to dichotomous sampler data sets for St. Louis, MO (Stevens et al., 1978; Dzubay, 1980; Alpert and Hopke, 1981), Charleston, WV (Stevens et al., 1978; Lewis and Macias, 1980), Denver, CO (Dzubay et al., 1981), Houston, TX (Dzubay et al., 1982) and several other cities (Stevens et al., 1978). Crustal EF for the coarse aerosol fraction (the lower size cut-off varying from 2.0-3.5 μm) ranged from 0.35-4.76 with an unweighted mean value of 1.9. For the fine fraction, values ranged from 1.83-36.8, with a mean of 14.4. The ratio crustal EF (fine fraction): crustal EF (coarse fraction), ranged from 2.02-28.9, with a mean of 8.1. Thus, it can be inferred by this rough illustration that manganese in coarse aerosol fractions tended to be associated with aluminum in ratios found in

crustal material. Lower relative concentrations of aluminum in fine fractions indicated a greater influence of noncrustal manganese sources in fine than in coarse particles in ambient aerosols.

The above conclusions were reached based on data sets which were averaged over time and/or local geography. However, a single sample from one St. Louis site (RAPS site 108) strongly influenced by steel processing showed an EF for the coarse fraction (16.9) slightly greater than that for the fine fraction (15.6) (Dzubay, 1980). Therefore, industrial processes may be expected to have local influence on manganese levels in the coarse particle fraction, but this influence is likely to be less pervasive than fine fraction enrichment, due to the more rapid deposition of the larger particles (Kleinman et al., 1975).

3.5. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

3.5.1. Principal Cycling Pathways and Compartments. Garrels et al. (1975) presented the pre-human cycle and the present-day cycle of manganese (Figure 3-1). Manganese, an element of low volatility, tends to settle out near sources of pollution and to be of concern in local or regional environmental problems. However, fine particulate materials containing manganese can be distributed world-wide. According to Garrels et al. (1975), the major exchange of manganese between the atmosphere and the pre-human earth surface was due to continental dust being swept into the atmosphere by winds and then falling back onto the earth's surface. Today this dust flux is augmented by manganese emitted to the atmosphere in particulate form by industrial activities. The total river flux of manganese to the ocean today is estimated to be nearly three times the pre-human flux. This increase represents principally an increase in the rate of stripping the land's surface from about 160×10^{14} g/year pre-human to today's rate of about



FLUXES 10^{10} g yr^{-1} ; RESERVOIR MASES 10^{10} g

FIGURE 3-1

The Global Cycles of Manganese

Source: Garrels et al., 1975

225×10^{14} g/year. Because this increase in stripping reflects an increase in the load of suspended solids to rivers from deforestation and agricultural activities, and because manganese is concentrated in the ferric oxide coatings on suspended material and in the suspended particles, the land-to-ocean manganese flux is higher today than in the past. Manganese in particulate emissions from industrial activities rivals the natural input of continental dust to the atmosphere. Most particulate manganese probably falls out of the atmosphere near industrial sources.

The mining of manganese ore has resulted in a net gain for the land reservoir and a net loss from the sediment reservoir. There is no evidence of change over time in dissolved manganese in the oceanic reservoir (Garrels et al., 1975).

3.5.2. Atmospheric Fate and Transport.

3.5.2.1. CHEMICAL FORMS PRESENT IN THE ATMOSPHERE -- Soils, dust and other crustal materials containing naturally-occurring manganese compounds enter the atmosphere as a result of natural and anthropogenic processes (see Section 3.4.1.). While a number of ores exist (see Table 3-9), the most common forms of manganese in rocks and soils are oxides and hydroxides, of oxidation states +2, +3 and +4, and manganese carbonate (Hem, 1970). These are undoubtedly the most common manganese compounds in the coarse particulates of crustal origin. Like soils, these particles usually contain manganese at concentrations of $\leq$1 mg/g ($\leq$0.1%) (see Section 3.4.1. and Tables 14, 15 and 16).

The manganese emitted by metallurgical processes is normally described as consisting of oxides (see Section 3.4.2.). Manganese from combusted MMT is emitted primarily as Mn_3O_4 (Ethyl Corporation, 1972). Much of the particulate released from these processes is in the fine range (<2.5 μm).

fine particulate from fly ash usually is no more highly enriched in manganese than are soils, but the fine particles arising from metallurgy and MMT combustion are enriched, with manganese concentrations ranging from 14-250 mg/g (1.4-25%) (see Sections 3.4.2., 3.4.3. and Tables 3-10 and 3-14)..

Minute amounts of organic manganese compounds may be present in ambient air under certain conditions. Ethyl Corporation (1972) analyzed the exhaust products of three cars operating on gasoline containing an abnormally high level of MMT (1.25 g Mn/gal). About 0.1-0.5% of the manganese burned was emitted in organic form. However, these authors found that MMT was rapidly photodegraded to inorganic manganese in sunlight; estimated half-life was 10-15 seconds. They estimated that, for cars meeting 1975 emissions standards and an MMT use rate of 0.125 g Mn/gal, ambient MMT concentration would be 0.12-0.48 ng MMT/m^3 (0.03-0.12 ng Mn/m^3) if photodegradation were neglected, and $\leq$0.048 ng MMT/m^3 ($\leq$0.012 ng Mn/m^3) if photodegradation were considered (Ter Haar et al., 1975).

Coe et al. (1980) used gas chromatography-atomic absorption spectrometry to measure MMT levels in air in Canada, where MMT is presently in use in unleaded fuels. With a detection limit of 0.1 ng MMT/m^3, they were unable to detect MMT in samples of auto exhaust from unleaded gasoline (emission control system unspecified). With a limit of 0.05 ng MMT/m^3, they could not detect MMT on Toronto streets. MMT detected in an underground car park at levels of 0.1-0.3 ng/m^3 was presumed to arise from fuel evaporation or spillage, rather than exhaust emissions (Coe et al., 1980).

3.5.2.2. ATMOSPHERIC REACTIONS -- Except for the photodegradation of MMT, very little information is available on the atmospheric reactions of manganese. Manganese dioxide can react with sulfur dioxide or nitrogen dioxide to form manganous sulfate ($MnSO_4$) and dithionate (MnS_2O_6) or

manganese nitrate [$Mn(NO_3)_2$], respectively (Hay, 1967; Schroeder, 1970). Various oxides of manganese (MnO, Mn_2O_3, MnO_2), used as absorbants, have been shown to combine with sulfur dioxide in heated flue gases (Bienstock and Field, 1960). The possibility of these reactions occurring in the atmosphere has been recognized (Sullivan, 1969; Piver, 1974) but occurrence or reaction rates have not been demonstrated.

It has been shown that aerosols of manganous sulfate can catalyze the oxidation of atmospheric sulfur dioxide to sulfur trioxide, thus promoting the formation of sulfuric acid (Matteson et al., 1969; Sullivan, 1969; Piver, 1974):

$$2SO_2 + O_2 \xrightarrow{MnSO_4} 2SO_3 \xrightarrow{+2H_2O} 2H_2SO_4$$

It has been reported that under foggy conditions, an atmospheric manganese concentration of 0.2 $\mu g/m^3$ and a sulfur dioxide concentration of 1750 $\mu g/m^3$ would result in a sulfuric acid formation rate of 25 $\mu g/m^3/hr$, or a conversion rate of 1.4%/hr (Bracewell and Gall, 1967; Sullivan, 1969). Extrapolations from the experimental data of Matteson et al. (1969) suggest that at concentrations of 259 μg SO_2/m^3 and 2 μg Mn/m^3, a rate of ~0.04%/hr would be observed (Wright et al., 1973).

A test was conducted to determine the catalytic effect of exhaust products from a car burning MMT-containing fuel on the disappearance of SO_2 in ambient air (Wright et al., 1973). In the absence of manganese, at a relative humidity of 90-100% and an SO_2 concentration of 35 $\mu g/m^3$, the rate constant for SO_2 disappearance was 14%/hr. This unusually high rate was attributed primarily to impaction on the black polyethylene bag in which the experiment was conducted. Addition of exhaust to give a manganese concentration of 4 $\mu g/m^3$, a level much higher than normally encountered

in ambient air (see Section 3.6.1.), did not noticeably affect this rate, although manganese concentrations >30 $\mu g/m^3$ did increase the rate constant. On the other hand, addition of 20 $\mu g/m^3$ of ammonia, an amount probably about equal to the ammonia already present in ambient urban air, caused the rate constant to double. The authors concluded that ambient ammonia was therefore the rate-controlling factor for SO_2 oxidation, and that addition of MMT to gasoline would have no measurable effect. This conclusion with respect to manganese is weakened by the apparent magnitude of the container effect, and because the control contained no exhaust, rather than manganese-free exhaust.

Hidy et al. (1977), in an unpublished analysis of this topic prepared for Ethyl Corporation, concluded that the manganese-induced acceleration of SO_2 oxidation was not truly catalytic, but occurred because the presence of Mn^{2+} enhanced the absorption of SO_2 by water droplets. In addition, since iron promotes SO_2 oxidation more efficiently than manganese, and is present at much higher ambient concentrations, these authors concluded that the effect of manganese on atmospheric sulfate formation is negligible and would not be appreciably magnified by changes in MMT use.

3.5.2.3. DRY AND WET DEPOSITION -- Atmospheric particulate matter, including manganese, is transported by air currents until it is lost from the atmosphere by either dry or wet deposition.

Dry deposition rate is strongly affected by particle size. Kleinman et al. (1975) studied the deposition of nine metals in New York City. Particle deposition velocity was calculated by comparing the amount deposited with the air concentration immediately above the collection surface. Deposition velocity was lowest (1.1 cm/sec) for lead, which was mainly associated with small particles [mass median aerodynamic diameter (MMAD) = 0.56 μm].

Manganese had highest velocity (10.4 cm/sec) and a larger particle size (MMAD = 1.3 μm). Dry deposition of manganese at three New York City sites averaged 300-670 ng/cm^2/month and ranged from 24-1700 ng/cm^2/month. Assuming total transfer of particulates to runoff, dry deposition resulted in an estimated manganese concentration in urban runoff of 39 μg/ℓ, or about 120 kg/day discharged to New York Harbor (Kleinman et al., 1975).

By comparison, average wet deposition of manganese in New York reported ly was 120 ng/cm^2/month, stemming from a rainfall concentration of 19 μg Mn/ℓ (Volchok and Bogen, 1973). Thus, manganese deposited in dustfall was more than twice that in rainfall.

Manganese deposition in precipitation at ~30 stations throughout the U.S. in September 1966-January 1967 was reported by Lazrus et al. (1970). Amounts deposited ranged from undetectable (<10 ng/cm^2/month), for Mauna Loa, Hawaii; Amarillo, Texas; and Tampa, Florida to levels of 200-300 ng/cm^2/month for Chicago, Illinois and Sault St. Marie, Michigan. An unusually high value of 540 ng/cm^2/month was observed in Caribou, Maine. The latter city is located in Aristook County, an area of low-grade manganese ore deposits. The average value nationwide was ~80 ng/cm^2/month, and the average manganese concentration in precipitation was ~12 μg/ℓ (Lazrus et al., 1970).

None of the above measurements was made in the immediate vicinity of a major industrial source. Dry deposition of manganese was measured in a 1964-1965 study of air pollution in the Kanawha Valley, West Virginia (NAPCA, 1970). In the two communities nearest a ferromanganese plant, manganese deposition averaged 19,300 and 2700 ng/cm^2/month, respectively. Deposition in other locations in the valley ranged from 80-320 ng/cm^2/month (see Section 3.6.1.2.).

3.5.3. Fate and Transport in Water and Soil.

3.5.3.1. CHEMICAL FORMS IN SOLUTION -- The aqueous chemistry of manganese is complex, as manganese can be present in II, III, IV, VI and VII oxidation states. Mn(II) and Mn (IV) are the oxidation states most commonly found. In neutral and acid aqueous solutions, the II state exists as the hexaquo ion, $[Mn(H_2O)_6]^{2+}$, which is unstable with respect to oxidation by O_2 over the entire pH range of natural water (Morgan, 1957). The maximum concentration of soluble Mn^{2+} in many natural waters is limited by the solubility product of $MnCO_3$. With low alkalinities and reducing conditions in freshwaters, solubility may be restricted by high sulfide concentrations.

The possible chelating influence of natural organic compounds in natural waters was studied on a hypothetical multimetal, multi-ligand system. Calculations were performed simultaneously by Morel and Morgan (1972) and by Stumm and Bilinski (1972), and both concluded that a free manganese ion may be present as a predominant species even if complex-forming organic matter is present.

In water or soil of pH >8 or 9, the soluble divalent manganese ion is chemically oxidized to the insoluble tetravalent form. At pH <5.5, chemical reduction of the tetravalent form takes place. However, the interconversion of these forms which is commonly observed at intermediate pH occurs only by microbial mediation (Alexander, 1977; Konetzka, 1977).

Groundwater has different manganese equilibria than surface water because of the oxygen-poor environment. Nichol et al. (1967) suggested that in acid, water-logged soils, manganese passes freely into solution and circulates in the groundwater. On entering stream waters with average pH and biological oxidation potential (E_h), manganese is precipitated, thus

giving rise to stream sediments enriched with manganese. Mitchell (1971) also showed that the mobilization of manganese was greatly enhanced in acid, poorly drained podzolic soils and groundwaters. Josephson (1980) found that manganese exists in a reduced state in groundwater and that it can be readily leached from waste sites or from natural sources. High levels of divalent manganese may also be found in acid mine drainage (see Section 3.6.2.).

Various opinions exist regarding the dominant form of manganese in seawater. According to Sillen (1961), the dominant form of manganese is $Mn(OH)_3$ or $Mn(OH)_4$. Moklevskaya (1961) and Spencer and Brewer (1971) found that in water of the Black Sea, the dominant form of manganese was the divalent form. Fukai and Huynh-Ngoc (1968) found that divalent manganese remained in that form in seawater for a long period of time. According to Breck (1974), the main species are MnO_2 and/or Mn_3O_4. Ahrland (1975) considered that dispersed $MnO_2(s)$ is predominant. Musani-Marazovic and Pucar (1977) concluded that ^{54}Mn introduced in divalent form into seawater behaves as a cation.

3.5.3.2. MICROBIAL TRANSFORMATION -- Bacteria are important agents in determining the form and distribution of metals in the environment. Alexander (1967) described how the availability of manganese in soil or water is affected by microorganisms. Several processes can occur: release of inorganic manganese ions during decomposition of organic material; immobilization of ions by incorporation into microbial tissue; oxidation of manganese to a less available form; direct, enzymatic reduction of oxidized manganese; or indirect transformation (especially reduction) through changes in pH or E_h. Saxena and Howard (1977) also concluded that bacteria play a major part in the modification, activation and detoxification of heavy metals.

For example, manganese usually enters a lake in the insoluble oxidized form, which settles to the sediment. Manganese-reducing bacteria may be active in the sediments, or manganese may be reduced by the lowering of pH resulting from general microbial activity (i.e., O_2 consumption or the production of acidic metabolites) (Kuznetsov, 1970; Alexander, 1977). In the first case the reduction is enzymatic; in the second it is nonenzymatic. Reduced manganese then diffuses upward in the sediment or into the water column. In Lake Parnus-Yarvi of the Karelian Isthmus (USSR), iron- and manganese-reducing bacteria are present in the upper 10 cm of the sediments. Reduced manganese in the bottom waters of the profundal zone reaches 1.4 mg/ℓ, whereas the total manganese concentration in the rest of the lake is only 0.01 mg/ℓ (Kuznetsov, 1970).

Several types of bacteria have been found capable of oxidizing manganese. The first are included among the "iron bacteria," or "that group of aerobic bacteria which appear to utilize the oxidation of ferrous and/or manganous ions as an essential component in their metabolic functioning" (Cullimore and McCann, 1977). These have been assumed to be chemoautotrophs, utilizing energy from the reduction of manganese to carry out synthetic processes (Kuznetsov, 1970), but others have questioned this conclusion (Alexander, 1977; Konetzka, 1977). A second group consists of heterotrophs possessing a slime capsule that can absorb divalent manganese. Oxidation then occurs within the sheath, which becomes impregnated with the hydroxide (Kuznetsov, 1970). Manganese-oxidizing ability has been shown to occur in a wide variety of freshwater bacterial genera, comprising from <1-69% of the heterotrophic bacterial population of two freshwater lakes studied (Gregory and Staley, 1982).

Divalent manganese entering the water column from the sediments is precipitated by these organisms, usually in the form of hydroxides. This leads to a repetition of the redox cycle. However, in lakes such as Pannus-Yarvi where bottom currents carry the reduced manganese out of the profundal zone and into more shallow and highly oxygenated areas, microbial oxidation in the sediments can lead to the formation of manganese lake ores (Kuznetsov, 1970).

Bacterial oxidation of Mn^{2+} has also been implicated in the formation of manganese nodules on the ocean floor (Silver and Jasper, 1977). However, this conclusion is far from certain, as some nodule-associated bacteria catalyze manganese accretion via oxidation while others catalyze manganese reduction (Ehrlich, 1972).

Iron bacteria can be a tremendous nuisance in water supply systems because of their tendency to foul pipes and other surfaces with iron or manganese oxides. This problem is especially acute in wells in many regions of the world. Most study of conditions contributing to these problems has focused on iron rather than manganese, and the role of the latter remains poorly understood (Cullimore and McCann, 1977). Luthy (1964) stated that 0.05 mg Mn^{2+}/ℓ is undesirable because of discoloration of the water, and that measures for bacterial control should be taken at levels >0.15 mg Mn^{2+}/ℓ. Control measures include sterilization of equipment before drilling of wells, and treatment of affected systems by chlorination, acidification, or other antibacterial agents (Cullimore and McCann, 1977).

In the soil, microorganisms play an important role in determining the availability of manganese to plants. Several genera of bacteria and fungi are capable of oxidizing soil manganese, many even under slightly acid conditions. Numerically, the manganese oxidizers may constitute up to 5-15%

of the total viable microflora. Addition of organic matter to soils can increase manganese oxidation by stimulating population increase of these groups (Timonin and Giles, 1952). Since the oxides are less available or unavailable to plants, symptoms of manganese deficiency may result (Alexander, 1977).

Regeneration of reduced manganese may be enzymatic or nonenzymatic, as in water. The reduction proceeds more rapidly in poorly drained soils. In such cases, manganese phytotoxicity may also occur (Alexander, 1977).

3.5.3.3. BIOCONCENTRATION -- The tendency of a substance to be concentrated in organisms will have an important effect on its ultimate distribution in biological and nonbiological ecosystem compartments. Figure 3-2 shows an example of concentration factors for manganese in an estuarine system (Hudson River), determined by Lentsch et al. (1972). They observed that filamentous algae have the greatest concentration factor, and the most predatory organism has the lowest concentration factor. They also observed that the higher organisms do not have higher concentration factors, as these seem to be capable of regulating manganese. Thus, biomagnification or increasing accumulation with trophic level evidently was not occurring.

3.6. ENVIRONMENTAL LEVELS AND EXPOSURE

3.6.1. Air.

3.6.1.1. NATIONWIDE TRENDS -- In 1953, the U.S. PHS initiated an air sampling program in 17 cities. Some samples were analyzed individually and others as quarterly composites. Twelve nonurban samples collected in 1955-1956 at Point Woronzof, Alaska, showed an average manganese concentration of 0.01 $\mu g/m^3$, with a maximum of 0.02 $\mu g/m^3$ (U.S. DHEW, 1958). Over 100 suburban samples collected at nine different locations in the United States in 1954-1956 averaged 0.06 $\mu g/m^3$, with a maximum value of

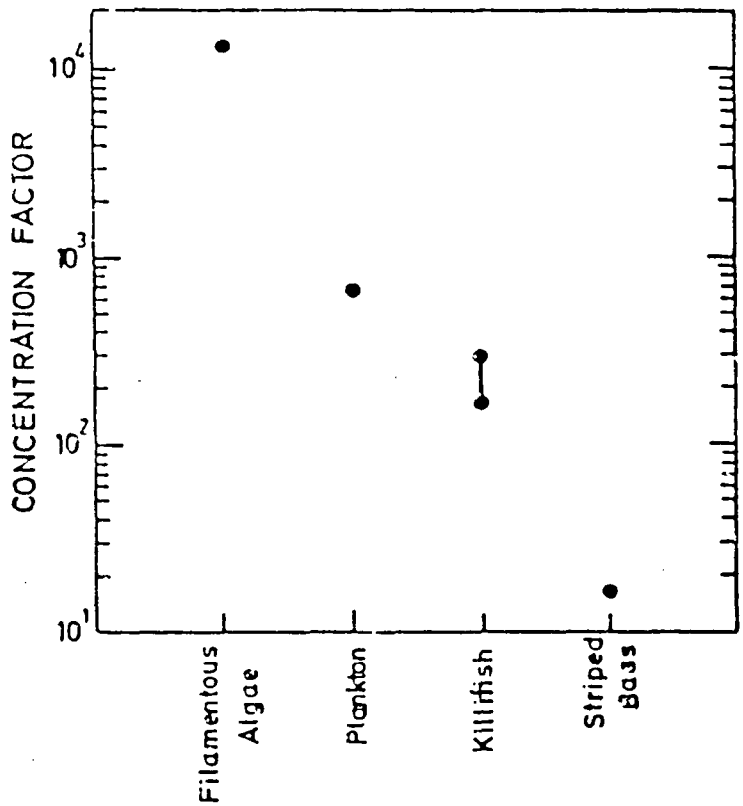


FIGURE 3-2

Concentration Factors for Manganese in Hudson River Aquatic Food Chain - June, 1970

Source: Lentsch et al., 1972

0.50 $\mu g/m^3$ in Kanawha County, West Virginia. Nearly 2000 urban samples collected in 1953-1957 averaged 0.11 $\mu g/m^3$, with a maximum value of 9.29 $\mu g/m^3$ at Cincinnati, Ohio in 1955. Concentrations $\geq$3.0 $\mu g/m^3$ were found in Anchorage, Alaska in 1954-1955, probably after volcanic eruption; in Philadelphia, Pennsylvania in 1954; and in Chattanooga, Tennessee in 1955-1956.

The National Air Surveillance Network started analysis January 1, 1957, at 26 randomly-selected stations 24 hours/day for 1 year. Comparison of data from different years involves problems because of changes in the analytical methodology and the number and position of stations. However, an examination of nationwide summaries of these data does permit a rough assessment of national trends.

The data for all NASN sites for 1957-1963 are summarized in Table 3-17. The sites are categorized into four concentration ranges. Since urban and nonurban data are not segregated and the majority of sites fall into the low range (<0.099 $\mu g/m^3$), this display serves primarily to show the number of urban sites with particularly high ambient manganese concentrations. A comparison of 1957-1963 data with post-1963 data shows a clear decline in the percentage of sites with concentrations >0.100 $\mu g/m^3$. Table 3-18 gives NASN sites for which average concentrations were $\geq$0.5 $\mu g/m^3$. Higher concentrations for shorter average times may be of considerable significance in the evaluation of the potential biological effects of airborne manganese. Several 24-hour values >10 $\mu g/m^3$ were observed during this time period (see Table 3-18).

A comparison of urban and nonurban NASN data for 1966-1967 was provided by McMullen et al. (1970). Urban samples showed an arithmetic mean manganese concentration of 0.073 $\mu g/m^3$, while the mean for nonurban samples decreased from 0.026 to 0.005 $\mu g/m^3$ with increasing remoteness of the

TABLE 3-17

Number of National Air Surveillance Network Stations within Selected Annual Average Manganese Air Concentration Intervals, 1957-1969*

Year	Number and Percent of Stations by Air Concentration Interval, $\mu g/m^3$ (percent shown in parentheses)				
	<0.099	0.100-0.199	0.200-0.299	>0.300	Total
1957-1963	76 (59.4)	29 (22.7)	10 (7.8)	13 (10.2)	128 (100)
1964	68 (73.1)	12 (12.9)	6 (6.5)	7 (7.5)	93 (100)
1965	132 (84.1)	14 (8.9)	5 (3.2)	6 (3.8)	157 (100)
1966	113 (88.3)	8 (6.3)	4 (3.1)	3 (2.3)	128 (100)
1967	121 (85.2)	13 (9.2)	4 (2.3)	4 (2.8)	142 (100)
1968	126 (86.9)	11 (7.6)	2 (1.4)	6 (4.1)	145 (100)
1969	169 (80.9)	23 (11.0)	9 (4.3)	8 (3.8)	209 (100)
1957-1969	805 (80.4)	110 (11.0)	40 (4.0)	47 (4.7)	1002 (100)

*Source: NASN, 1957-1969

TABLE 3-18

National Air Surveillance Network Stations with
Annual Average Manganese Air Concentrations
Greater than 0.5 $\mu g/m^3$*

Year	Station	Manganese Concentration, $\mu g/m^3$		
		Average	Maximum Quarterly	Maximum 24-hour
1958	Charleston, WV	0.61	1.10	7.10
1959	Johnstown, PA	2.50	5.40	7.80
	Canton, OH	0.72	1.10	2.20
1960	Gary, IN	0.97	NR	3.10
1961	Canton, OH	0.57	NR	2.90
	Philadelphia, PA	0.70	NR	>10.00
1963	Johnstown, PA	1.44	NR	6.90
	Philadelphia, PA	0.62	NR	3.70
1964	Charleston, WV	1.33	NR	>10.00
1965	Johnstown, PA	2.45	3.90	NR
	Philadelphia, PA	0.72	1.70	NR
	Lynchburg, VA	1.71	2.50	NR
	Charleston, WV	0.60	1.70	NR
1966	Niagara Falls, NY	0.66	1.30	NR
1967	Knoxville, TN	0.81	1.50	NR
1968	Johnstown, PA	3.27	NR	14.00
1969	Niagara Falls, NY	0.66	1.30	NR
	Johnstown, PA	1.77	2.10	NR
	Philadelphia, PA	0.50	1.30	NR

*Source: NASN, 1957-1969

NR = Not reported

monitoring site from urban areas (Table 3-19). While this decrease of manganese concentration primarily reflects a decrease in total suspended particulates, percent manganese in TSP mass also decreased with increasing remoteness (McMullen et al., 1970).

An examination of NASN data for the early 1970s shows a further decline in ambient manganese levels at urban sites, and indicates some reduction at nonurban sites as well. The U.S. EPA (1977a) reported that the median (50th percentile) value of annual average manganese concentrations for 92 urban sites declined from 0.040 $\mu g/m^3$ in 1965 to 0.016 $\mu g/m^3$ in 1974. When urban values for the period 1970-1971 were compared to those for 1973-1974, a 50% decline was observed in both the 50th and 90th percentile values for manganese, indicating a reduction by about half in both median and extreme levels. During this same interval, the reductions in TSP at these percentiles were only 4% and 13%, respectively, indicating that this reduction was not simply related to a general improvement in air quality. The trend for manganese was thought to be attributable to controls in the metals industry. Data examined for 16 nonurban sites were also said to indicate a downward trend for manganese, but this conclusion was described as tenuous (U.S. EPA, 1977a).

The frequency distributions of quarterly analytical values for manganese at all urban and nonurban NASN sites for the years 1970-1982 are given in Table 3-20 and 3-21, respectively. Prior to 1977, quarterly values were based on single analyses of filter composites (U.S. EPA, 1979a). Since 1977, individual filters were analyzed. Therefore, to permit comparison of these data with the earlier data, quarterly arithmetic means of all values for each site were used to simulate quarterly composite values in the frequency distributions (Barrows, 1983). A rigorous trend analysis of these

TABLE 3-19

Average Manganese Concentration in Ambient Air and Total Suspended Particulates (TSP) in Urban and Nonurban NASN Sites, 1966-1967*

Stations		TSP	Mn	Mn/TSP
Type	Number	($\mu g/m^3$)	($\mu g/m^3$)	(%)
Urban	217	102	0.073	0.07
Nonurban				
Proximate	5	45	0.026	0.06
Intermediate	15	40	0.012	0.03
Remote	10	21	0.005	0.02
Total nonurban	30	34.5	0.012	0.03

*Adapted from McMullen et al., 1970

TABLE 3-20

Urban NASN Sites, 1970-1982: National Cumulative Frequency Distributions of Quarterly Values for Manganese Concentration ($\mu g/m^3$)[a,b]

Year	Number[c]	Minimum	Percentiles							Maximum	Arithmetic		Geometric	
			10	30	50	70	90	95	99		Mean	Standard Deviation	Mean	Standard Deviation
1970	795	LD[d]	0.02	0.03	0.04	0.06	0.15	0.23	0.49	2.10	0.07	0.12	0.04	3.13
1971	716	LD	0.02	0.04	0.05	0.07	0.16	0.24	0.46	1.95	0.08	0.11	0.05	2.81
1972	708	LD	0.01	0.02	0.03	0.04	0.09	0.12	0.22	0.86	0.04	0.06	0.03	2.76
1973	559	LD	0.01	0.02	0.02	0.04	0.07	0.11	0.29	0.56	0.04	0.05	0.02	2.72
1974	594	LD	0.01	0.02	0.02	0.04	0.07	0.11	0.21	0.35	0.04	0.04	0.02	2.39
1975	695	LD	0.01	0.02	0.03	0.04	0.07	0.10	0.18	0.72	0.04	0.04	0.02	2.49
1976	670	LD	0.01	0.02	0.03	0.04	0.08	0.12	0.27	0.74	0.04	0.05	0.03	2.60
1977	741	0.0051	0.017	0.025	0.032	0.045	0.077	0.100	0.297	0.632	0.045	0.051	0.034	2.486
1978	568	0.0043	0.016	0.025	0.034	0.043	0.088	0.111	0.185	0.300	0.043	0.035	0.034	2.043
1979	429	0.0022	0.011	0.017	0.025	0.035	0.073	0.102	0.158	0.448	0.035	0.039	0.026	2.443
1980	437	0.0039	0.009	0.015	0.021	0.031	0.063	0.093	0.133	0.141	0.030	0.026	0.022	2.111
1981	477	0.0040	0.011	0.017	0.024	0.033	0.059	0.084	0.138	0.303	0.032	0.030	0.025	2.214
1982	309	0.0031	0.011	0.017	0.023	0.032	0.063	0.081	0.170	0.661	0.033	0.047	0.024	2.846

[a]Source of 1970-1976 data: U.S. EPA, 1979a

[b]Source of 1977-1982 data: Barrows, 1983

[c]Number of quarterly site values. From 1-4 quarterly values were available per site.

[d]Limits of discrimination (LD) for 1970-1976 were ≈0.0025 $\mu g/m^3$, but varied among years. LD for 1977-1982 ranged from 0.00042-0.0024 $\mu g/m^3$.

TABLE 3-21

Nonurban NASN Sites, 1970-1982: National Cumulative Frequency Distributions of Quarterly Values for Manganese Concentration ($\mu g/m^3$)[a,b]

Year	Number[c]	Minimum	Percentiles							Maximum	Arithmetic		Geometric	
			10	30	50	70	90	95	99		Mean	Standard Deviation	Mean	Standard Deviation
1970	124	LD[d]	0.003	0.006	0.012	0.018	0.035	0.041	0.066	0.068	0.015	0.013	0.012	2.11
1971	97	LD	0.003	0.009	0.013	0.022	0.032	0.041	0.064	0.102	0.018	0.015	0.013	2.09
1972	137	LD	LD	LD	0.003	0.007	0.016	0.029	0.039	0.046	0.007	0.009	0.003	2.81
1973	100	LD	LD	LD	0.002	0.004	0.011	0.022	0.030	0.030	0.004	0.005	0.002	2.79
1974	79	LD	LD	0.001	0.004	0.007	0.017	0.023	0.027	0.033	0.006	0.007	0.004	2.52
1975	98	LD	LD	0.004	0.006	0.009	0.014	0.018	0.031	0.040	0.007	0.007	0.015	2.19
1976	99	LD	LD	0.005	0.007	0.010	0.025	0.030	0.036	0.046	0.010	0.009	0.010	2.21
1977	126	-0.0010	0.003	0.005	0.009	0.012	0.021	0.030	0.049	0.122	0.012	0.013	0.008	2.468
1978	85	0.0011	0.003	0.006	0.008	0.010	0.015	0.018	0.030	0.036	0.009	0.006	0.007	1.810
1979	44	-0.0010	0.002	0.004	0.005	0.007	0.011	0.015	0.024	0.024	0.005	0.006	0.005	1.862
1980	35	-0.0010	-0.001	0.004	0.005	0.007	0.014	0.018	0.019	0.019	0.007	0.005	0.005	1.970
1981	43	-0.0010	0.003	0.004	0.006	0.009	0.015	0.021	0.025	0.025	0.008	0.006	0.007	1.897
1982	33	-0.0010	0.001	0.003	0.005	0.007	0.009	0.009	0.015	0.015	0.005	0.003	0.004	1.907

[a]Source of 1970-1976 data: U.S. EPA, 1979a

[b]Source of 1977-1982 data: Barrows, 1983

[c]Number of quarterly site values. From 1-4 quarterly values were available per site.

[d]Limits of discrimination (LD) for 1970-1976 were ±0.0025 $\mu g/m^3$, but varied among years. LD for 1977-1982 ranged from 0.00042-0.0024 $\mu g/m^3$.

data is not possible due to changes in sites and methodology. Decreases over the period are indicated, however, both in median and extreme concentrations, for both urban and rural areas.

3.6.1.2. AREA STUDIES -- Pollution problems and trends can also be characterized on a more local scale. A few area studies in which ambient manganese concentrations are given will be discussed. In 1964-1965, a study was undertaken of air pollution in the Kanawha Valley, West Virginia (NAPCA, 1970). Average TSP levels for sites in the area ranged from 132-413 $\mu g/m^3$, compared to the national urban average of 100 $\mu g/m^3$ (Table 3-22). Yearly average suspended manganese concentrations were as high as 8.3 $\mu g/m^3$, with quarterly composite samples ranging up to 11.0 and 13.0 $\mu g/m^3$ for the Smithers and Montgomery communities, respectively. The major manganese source was a ferromanganese plant, with additional contributions from a large coal-burning industrial steam-generation plant (NAPCA, 1970). However, NASN data collected 11 years later (1976) in two Kanawha Valley communities (although not necessarily the same sampling sites) indicate decreases of an order of magnitude in ambient manganese concentration (see Table 3-22; U.S. EPA, 1979a).

A nearby region along the Ohio River between Marietta, Ohio and Parkersburg, West Virginia was studied during the period 1965-1966 (U.S. DHEW, 1967). Air quality in this area was influenced by a large plant producing manganese metals and alloys. Sampling of ambient particulate using a directional sampler or during different wind directions showed that for sites both north (Marietta) and south of the plant (Vienna, Parkersburg), ambient manganese concentration was always substantially higher when the wind was blowing from the direction of the plant (Table 3-23). The trend for TSP was not nearly so clear, however. Manganese levels as high as 11.4 $\mu g/m^3$ were observed in 24-hour samples downwind of the plant. At one site, a

TABLE 3-22

Manganese Concentrations in Air, Kanawha Valley Area, West Virginia[a]

Sampling Site and Site Number	TSP (µg/m³) Study Period Average	Suspended Manganese (µg/m³) Quarterly Composites						Settled Manganese (ng/cm²/month)
		Fall 1964	Winter 1964-1965	Spring 1965	Summer 1965	Study Period Average	Yearly Average[b] 1976	Study Period Average
Falls View (1)	179		3.40					
Smithers (5)	347	11.00	6.50	4.50	3.00	8.30		19,300
Montgomery (6)	413		13.00					2,700
Cedar Grove (7)	235	4.20	3.50	1.80	0.32	2.45		130
Marmet (11)	242		3.60					110
Kanawha City (13)	287	3.30	1.10	0.53	0.27	1.30		80
Charleston (15)	189		0.91				0.07	
West Charleston (17)	209		0.96					
North Charleston, West (19)	241		0.52					240
South Charleston, East (20)	298	2.00	0.26	0.23	0.17	0.67	0.04	320
Dunbar (22)	199		0.24					
St. Albans (24)	223	0.43	0.44	0.06	0.06	0.25		80
Nitro (25)	179	0.59	0.28	0.10	0.09	0.27		90
Nitro, West (27)	132		0.08					

[a]Source: KAPCA, 1970

[b]Source: U.S. EPA, 1973a. NASN data, not necessarily same sampling locations.

TABLE 3-23

Ambient Air Sampling Data for Total Suspended Particulates and Manganese (in $\mu g/m^3$) in the Marietta, OH-Parkersburg, WV Vicinity, 1965-1966[a] and 1982-1983[b]

Site	Nov. 3, 1965[a]		Nov. 27, 1965[a]		Jan. 15, 1966[a]		Jan. 25, 1966[a]		Composite, Jan. 11-31, 1966[a]		Mean (Range), Dec. 1982-Feb. 1983[b]	
	TSP	Mn	TSP	Mn	TSP	Mn	TSP	Mn	TSP	Mn	TSP	Mn
Vienna											47 (12-97)	0.14 (0.03-0.56)
In[c]					196[d]	3.4[d]	278[d]	2.0[d]	197	4.1		
Out[c]					54[d]	0.1[d]	128[d]	0.2[d]	83	0.4		
Marietta (Central)	257[d]	1.6[d]	121[d]	1.6[d]	67[e]	0.1[e]	155[e]	0.1[e]	132	0.6		
Marietta (West)	309[d]	11.4[d]	204[d]	6.6[d]							32 (20-48)	0.13 (0.03-0.51)
Parkersburg (Central)	163[e]	0.29[e]	81[e]	0.0[e]	124[d]	0.7[d]	219[d]	0.7[d]	134	0.7		

[a]Source: U.S. DHEW, 1967

[b]Source: Unpublished data of Elkem Metals Co., Marietta, OH (Moore, 1983b)

[c]Directional sampler; "In": 90° sector toward ferromanganese plant; "Out": remaining 270° sector

[d]Site was downwind of ferromanganese plant during sampling period

[e]Site was upwind of ferromanganese plant during sampling period

composite of samples collected by a directional sampler selective for wind direction showed manganese levels 10 times higher for the 90° sector toward the plant (4.1 $\mu g/m^3$) than for the remaining 270° sector (0.4 $\mu g/m^3$). Recent unpublished monitoring data for two of these sites have been provided by the current operator of the manganese plant (Moore, 1983a,b). The mean and range of at least 14 24-hour samples during the winter (December 2-February 4) of 1982-1983 indicate substantial reductions (by roughly an order of magnitude) in manganese when compared with data from the earlier study (see Table 3-23). TSP levels were also reduced. Manganese production rates at this plant during the recent sampling period were reported to be 60-70% of those for 1965-1966 (Moore, 1933b).

Ambient manganese levels in New York City are substantially lower than those in areas influenced by the manganese metal and alloy manufacturing industry. However, trends can be noted here as well. Data of Kleinman et al. (1980) for NYU Medical Center and a location in the Bronx show substantial reductions in annual averages for manganese and several other metals during the years 1968-1975 (Table 3-24). The greatest decrease was observed over the years 1968-1972. TSP levels measured at the Medical Center showed that the decrease was concomitant with a decrease in TSP.

3.6.1.3. PARTICLE SIZE -- Techniques for accurately characterizing particle-size distributions for trace metals in ambient particulate matter have been available and improving since about 1970. Lee et al. (1972) used cascade impactors to achieve a size fractionation of ambient aerosols in six United States cities during 1970. Their data showed that, on an annual average, 45-62% of ambient manganese was in particles of ≤ 2 µm diameter. Bernstein and Rahn (1979) used a size-selective cyclone sampler to fractionate New York City urban aerosol during 2 weeks of sampling in August, 1976.

TABLE 3-24

Concentrations of Trace Metals in Air Measured at Three Locations in New York City* (ng/m^3)

	New York University Medical Center				
Element	1969	1972	1973	1974	1975
Cd	10.0	6.0	7.1	6.0	4.2
Cr	33.0	11.9	8.9	10.8	8.5
Cu	526	63.0	55.7	46.8	43.9
Fe	NR	1490	1580	1410	1010
K	NR	240	358	371	99.1
Mn	89.0	27.5	28.1	23.1	19.8
Na	NR	1130	1990	604	800
Ni	1390	30.7	45.0	45.4	35.2
Pb	2110	1370	1240	1400	1070
V	874	68.9	86.0	72.6	38.8
Zn	670	380	311	338	294
TSP ($\mu g/m^3$)	134	82	80	71	52

	Bronx, New York			
Element	1968	1969	1972	1973
Cd	14.0	9.0	4.0	3.5
Cr	49.0	23.0	7.0	5.3
Cu	133	115	60.0	52.5
Fe	NR	NR	1940	1440
K	NR	NR	NR	NR
Mn	54.0	40.0	29.0	30.2
Na	NR	NR	NR	NR
Ni	150	122	210	311
Pb	3820	2760	2000	1580
V	1230	795	53.0	80.0
Zn	730	1120	304	289

*Source: Kleinman et al., 1980

NR = Not reported

In these samples, 64-68% of manganese was found in particles of <2.5 μm diameter. Manganese was bimodally distributed, with a peak in the 0.5-1.5 μm fraction, a nadir in the 1.5-2.5 μm fraction, and a second peak in the 2.5-3.5 μm fraction. A single week of sampling with this device in November, 1974, had shown only the latter (2.5-3.5 μm) peak (Bernstein et al., 1976).

More recent data tend to indicate that less of the ambient manganese is found in fine particles. Dichotomous samplers, which segregate particles into fine and coarse fractions, have been used widely since about 1975. Davis et al. (unpublished manuscript) performed analyses of 104 selected filter pairs from dichotomous samples collected in 22 geographically diverse cities in the United States during 1980. The size classes were <2.5 μm (fine) and 2.5-15 μm (coarse). Filters with a high level of total particulate were selected to facilitate analysis. Therefore, the sample has some bias, and the concentrations are not representative. However, this was considered an excellent data base for examining relative amounts of manganese in fine and coarse aerosol.

Table 3-25 shows that the manganese concentration (in mg/g) in particles of each fraction is highly variable, but tends to be higher in the coarse particles. Since coarse particle mass also tends to be greater, the overall precentage of manganese found in fine particles tends to be <50% of the total measured; the average for this study was 28%.

The total particulate measured by the dichotomous sampler (DS) with a 15 μm size-selective inlet is less than the TSP measured by high-volume samplers. The ratio DS:TSP has been measured for samples where TSP is >55 $\mu g/m^3$ (Pace and Frank, 1983). Ninety percent of all values for the ratio were between 0.36 and 0.76; the mean was 0.56. The ratio is somewhat

TABLE 3-25

Selected Dichotomous Sampler Data on Manganese and Particle Mass from 22 U.S. Cities in 1980[a]

Parameter[b]	Manganese		Particle Mass	
	Mean[c]	Range	Mean[c]	Range
Air concentration ($\mu g/m^3$)				
Fine	0.016	0.001-0.085	28.7	9.7-57.1
Coarse	0.030	0.003-0.078	44.6	8.2-105.6
Total	0.045	0.006-0.129	73.3	36.0-140.4
Particle concentration (mg/g)				
Fine	0.50	0.029-2.36	--	--
Coarse	0.70	0.27-1.75	--	--
Percent mass in fine fraction	28	3-66	41	15-78

[a]Source: Davis et al., unpublished manuscript

[b]Particle size: fine, <2.5 μm; coarse, 2.5-15 μm

[c]Arithmetic mean by city

higher when TSP is lower. If manganese is assumed to be distributed fairly evenly over particle mass for particles of different sizes, then this ratio can be used to compare dichotomous-sampler manganese with high-volume-sampler manganese. The percentage of manganese present in the fine fraction would then have an average of 28% x 56%, or 16%, of the total measured. However, since the manganese concentration (in mg/g) in coarse particles tends to be higher than in fine particles, this average is probably too high.

This indicates that only a small percentage of the manganese measured by the high-volume sampler usually is present in the fine fraction. However, it should be noted that of the 22 cities examined in this study, the city (Akron, OH) with the highest manganese concentration (0.129 $\mu g/m^3$) also had the highest percentage in the fine fraction (66%). Therefore, in high-exposure situations the relative amount in the fine fraction may be large. If the DS:TSP ratio was also high (e.g., 0.76), the percentage could be as high as 66% x 76%, or 50%.

3.6.2. Water. Natural concentrations of manganese in seawater are reported to vary from 0.4-10 µg/ℓ (U.S. EPA, 1975). Kopp and Kroner (1969) studied trace metals in United States freshwaters and generalized that "in most natural waters, the concentration of manganese is <20 µg/ℓ". In surface freshwaters, background levels are frequently exceeded due to human activities. Manganese concentration ranges in various United States lakes and rivers, some heavily polluted, are given in Table 3-26.

Kopp and Kroner (1969) summarized trace-element data for 1577 water samples collected over the contiguous United States and Alaska from 1962-1967, under the water quality surveillance program of the Federal Water Pollution

TABLE 3-26

Concentration of Manganese in Various Lake and River Waters

Locality	Concentration Range (µg/ℓ)	Reference
Wisconsin Lakes	3-25	Juday et al., 1938
Mississippi River	80-120	Wiebe, 1930
Linsley Pond, Connecticut	50-250	Hutchinson, 1957
Maine Lakes	0.02-87.5	Kleinkopf, 1960
Yukon River, Alaska	181	Durum and Haffty, 1963
Mississippi River	12-185	Durum and Haffty, 1963
Southeastern Missouri Streams	10-2420	Gale et al., 1973

Control Administration (FWPCA). Dissolved manganese was detected in 810 of 1577 samples; the mean concentrations of dissolved manganese for 16 drainage basins are shown in Table 3-27.

Manganese oxides are common constituents of suspended materials and frequently comprise >0.1% (>1000 µg/g) of riverine sediments (Hem, 1970). A comparison of suspended and dissolved manganese in Table 3-28 shows that, in river systems, the amount in suspension normally exceeds the amount in solution. Exceptions to this pattern are the Allegheny and Monongahela Rivers, which are characterized by acid mine drainage (Kopp and Kroner, 1969).

Manganese levels in groundwaters frequently are much higher than in surface waters because the more acid and reducing conditions which prevail in the sub-surface environment promote dissolution of manganese oxides. Manganese concentrations as high as 9600 µg/ℓ in acid groundwater (pH=4.0) and 1300 µg/ℓ in neutral groundwater (pH=7.0) have been reported (Hem, 1970).

In a 1962 U.S. Geological Survey study of public water supplies of the 100 largest cities in the United States, Durfor and Becker (1964) reported manganese concentrations of up to 2500 µg/ℓ for treated water. Of these water supplies, 97% contained concentrations below 100 µg/ℓ. A U.S. Public Health Service (U.S. PHS) community water survey in 1969 examined 2595 samples of tap water from 969 community water supplies (U.S. DHEW, 1970). The maximum concentration of manganese was 1320 µg/ℓ, but 91.9% of samples and 91% of supplies did not exceed 50 µg/ℓ.

As part of the first Health and Nutrition Examination Study (HANES I Augmentation Survey of Adults), conducted in 1974-1975, tap water samples from public and private water supplies of 35 urban and rural, randomly

TABLE 3-27

Mean Concentrations of Dissolved Manganese by Drainage Basin*

Drainage Basin	µg Mn/ℓ
Northeast	3.5
North Atlantic	2.7
Southeast	2.8
Tennessee River	3.7
Ohio River	232.0
Lake Erie	138.0
Upper Mississippi	9.8
Western Great Lakes	2.3
Missouri River	13.8
Southwest-lower Mississippi	9.0
Colorado River	12.0
Western Gulf	10.0
Pacific Northwest	2.8
California	2.8
Great Basin	7.8
Alaska	18.0

*Source: Adapted from Kopp and Kroner, 1969

TABLE 3-28

Dissolved and Suspended Manganese in Five U.S. Rivers*

Location	Dissolved		Suspended	
	Detection Frequency (%)	Mean of Positive Values (µg/ℓ)	Detection Frequency (%)	Mean of Positive Values (µg/ℓ)
Delaware River				
At Martins Creek, PA	40	2.9	93	18
At Trenton, NJ	27	3.2	100	57
At Philadelphia, PA	31	4.2	100	68
Allegheny River				
At Pittsburgh, PA	60	>1000	100	205
Monongahela River				
At Pittsburgh, PA	93	690	87	73
Ohio River				
Below Addison, OH	51	57	100	238
Kanawha River				
At Winfield Dam, WV	87	44	100	35

*Source: Kopp and Kroner, 1969

chosen sampling areas were analyzed for trace metals (U.S. DHEW, 1978). Unpublished data for manganese (Table 3-29) indicate that higher manganese concentrations can be found in private wells than in public water supplies (Greathouse, 1983). Manganese concentration at the 95th percentile was 3 times higher in private (228 µg/ℓ) than in public supplies (78 µg/ℓ). The median level for private supplies was below detection limits while that for public supplies was 4 µg/ℓ; however, since the detection limit was calcium dependent (U.S. EPA, 1978b) and may have been higher for private waters, the median levels may not be comparable to one another.

3.6.3. Food. Manganese concentrations were measured in foods from the United States (Schroeder et al., 1966; Daetz and Kenner, 1975; Wong et al., 1978), Great Britain (Wenlock et al., 1979) and New Zealand (Guthrie, 1975). Concentrations varied widely among food groups, within food groups, and even for a given food type. Concentrations in various grains and cereals in the United States ranged from 1.17-30.76 µg/g. Manganese concentrations for unpolished rice were given as 2.08 (United States), 32.5 (New Zealand) and 40 µg/g (Great Britain). Most non-cheese dairy products contained <1 µg/g, but cheeses varied widely. Swiss cheese in the United States was reported to contain 1.32 and 17.2 µg/g, respectively, by two different authors. Most meat, poultry and fish contained manganese at <2 µg/g. Most fresh fruits contained <2 µg/g, but bananas and canned fruits ranged from this level to 19 and 10 µg/g, respectively. The manganese content of various vegetables ranged from 0.14-12 µg/g. Most nuts contained from 7-35 µg/g, and certain spices (cloves, ginger, sage) contained >200 µg/g. Thus, it is obvious that wide differences in manganese intake can exist for people with differing or even with similar food habits.

3.6.4. Human Exposure. Data on manganese levels in air, water and food can be used to estimate human exposure to manganese. No attempt has been

TABLE 3-29

Cumulative Frequency Distribution of Manganese Concentration
in Tap Waters Sampled in the HANES I Augmentation Survey of Adults*

		Percentiles (µg/ℓ)					
Supply Type	Number	25	50	75	90	95	99
Public	2853	ND	4	13	36	78	295
Private	596	ND	ND	34	121	228	977

*Source: Unpublished EPA data (Greathouse, 1983)

ND = Less than detection limits (see text)

made in this document to project numbers of individuals subject to given exposure levels. Rather, manganese intakes characteristic of an "average" and a "high" level of exposure are estimated. These estimates are presented solely as a rough basis for comparison with the information on health effects in the following chapters.

3.6.4.1. INHALATION -- The degree of intake or absorption associated with human inhalation exposure to an aerosol is highly dependent upon particle size. Particles of diameter >100 μm can be inhaled, but few of those larger than ≈15 μm are likely to reach the thoracic region (U.S. EPA, 1982b). Insoluble particles deposited in the extrathoracic region are usually cleared to the esophagus within minutes, offering little opportunity for absorption of toxic constituents by the respiratory tract (although absorption by the digestive tract is possible; see Section 3.6.4.2.). Particles of smaller diameter may be deposited in the thoracic (i.e., tracheobronchial and alveolar) regions, to a degree which is dependent on type of breathing (i.e., oral or nasal), breathing flow rate, and particle characteristics. Insoluble particles deposited in the tracheobronchial region normally are cleared within hours, whereas those deposited in the alveolar region would be expected to remain for weeks, months or longer (U.S. EPA, 1982b).

Particles of ≈10 μm are almost all deposited extrathoracically during nasal breathing. During mouth breathing ≈35% are deposited tracheobronchially, but still practically none reach the alveoli. As particle size decreases, the fractions reaching the thoracic region and passing to the alveoli increase. Alveolar deposition is greatest (≈25-65%) for particles in the range of 2-4 μm. Nearly all particles smaller than 2 μm reach the alveoli, but many (≈50-80%) remain suspended and are

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exhaled (U.S. EPA, 1982). However, some conventions conservatively assume that none is exhaled; thus, >80% of particles smaller than 2 μm are considered to be deposited in the alveoli, and for particles ≈4-10 μm, <30% are alveolar and >50% are deposited in the tracheobronchial region (Ad Hoc Working Group of Tech[illegible] Committee 146-Air Quality, International Standards Organization, 1981).

Data collected by dichotomous sampler are roughly amenable to exposure estimates. The extrathoracic fraction is approximately excluded by an upper size cut-off, usually ≈15 μm. Thus, all aerosol sampled is assumed to reach the thoracic region. The coarse aerosol from the dichotomous sampler is generally taken to represent the tracheobronchial fraction, and the fine aerosol to be the alveolar fraction (Dzubay and Stevens, 1975). This assumption is a reasonable approximation if all particles reaching the alveoli are assumed to be deposited, as mentioned above. In actuality, as also has been discussed, the mode of the alveolar deposition curve is at 2-4 μm, and is usually divided by the size cut between fine and coarse fractions. However, for the purposes of this document, the conservative and simplifying assumptions will be made that the fine fraction is 100% deposited in the alveoli, and the coarse fraction is 100% deposited in the tracheobronchial region.

The NASN monitoring data were collected using high-volume samplers, which sample 50% of particles of 30 μm and some particles of up to 100 μm (Pace and Frank, 1983). Dichotomous sampler data from around the country indicate that of the manganese sampled (particles 0-15 μm), an average of ~28% and a maximum of ~66% is in the fine (≤2.5 μm) fraction (Davis et al., unpublished manuscript; see Section 3.6.1.3.). The dichotomous sampler collects an average of ~56% and a maximum of ~76% of

the TSP collected by the high-volume sampler (Pace and Frank, 1983; see Section 3.6.1.3.). Assuming similar percentages for manganese, and assuming daily inhalation of 20 m^3 of air, human inhalation exposure to manganese can be estimated from NASN data as follows:

Alveolar deposition (μg/day) = Ambient concentration (μg/m^3)

X Fine/DS X DS/TSP X 20 m^3/day

Total thoracic deposition (μg/day) = Ambient concentration (μg/m^3)

X DS/TSP X 20 m^3/day

where Fine/DS = Fine-fraction manganese/total dichotomous-sampler manganese and DS/TSP = Dichotomous-sampler particulate/high-volume-sampler particulate. Both alveolar and total thoracic deposition are estimated since both could have some role in causing adverse effects. Both average and maximum values for ambient concentration, Fine/DS, and DS/TSP are used for estimating average and maximum exposures.

The most recent (1982) ambient air monitoring data for the urban United States show a median quarterly manganese level of 0.023 μg/m^3, and a high quarterly value of 0.661 μg/m^3 (see Table 3-20). Ambient levels reaching ~10 μg/m^3 were observed near sites of manganese alloy manufacture during the 1960s (U.S. DHEW, 1967; NAPCA, 1970). These levels are of interest because they are relatively recent and could have had some bearing on health studies conducted during or subsequent to that period. However, such levels evidently are no longer occurring in ambient air.

Exposure estimates derived from these data are presented in Table 3-30. Alveolar deposition of manganese at current ambient levels is estimated as 0.072 μg/day (average) and 6.6 μg/day (high). Estimates of total thoracic deposition are slightly higher. Alveolar and total thoracic deposition under high exposure conditions in the 1960s were estimated to be as high as 100 and 152 μg/day, respectively.

TABLE 3-30

Estimates of Human Inhalation Exposure to Manganese in Ambient Air*

Exposure Type	Deposition Site	Ambient Concentration ($\mu g/m^3$)	Fine/DS	DS/TSP	Inhalation (m^3/day)	Exposure (μg/day)
1982 average	alveolar	0.023	0.28	0.56	20	0.072
	total thoracic	0.023	--	0.56	20	0.26
1982 high	alveolar	0.661	0.66	0.76	20	6.6
	total thoracic	0.661	--	0.76	20	10.0
1960s high	alveolar	10	0.66	0.76	20	100
	total thoracic	10	--	0.76	20	152

*See text for explanation and qualifications.

3.6.4.2. INGESTION -- Humans ingest manganese from three main sources: diet, drinking water and inhaled particles cleared from the respiratory tract.

No recommended daily allowance has been established for manganese, although it is recognized as essential (U.S. FDA, 1978). Various estimates have been made of average daily dietary intake of manganese by adults in the United States (Table 3-31); most recently, average consumption was estimated by the U.S. FDA (1978). This estimate was based on a market basket survey of 117 frequently eaten foods (the "Total Diet -- Adult") collected in 1976 in four United States geographic regions. The diet, including drinking water, was analyzed for several minerals, including manganese. Results expressed in terms of caloric intake were 1.28 mg Mn/1000 Calories. At the 3000 Calorie/day intake recommended for a 15 to 18-year-old male, average manganese intake would be 3.8 mg/day. Assuming a body weight of 70 kg, this amounts to an intake of ~0.054 mg/kg/day. It should be kept in mind that substantial variability in real intake levels is expected, as discussed in Section 3.6.3. The daily intake of manganese by bottle and breast-fed infants is much lower because of the low concentrations of manganese in both breast and cow's milk (Table 3-32). Manganese intake increases with age, as the type of feeding changes, from 0.002-0.004 mg/kg/day in infants, to 0.06-0.08 mg/kg/day in children.

In public water supplies, the median manganese concentration at the tap is 4 µg/ℓ (see Table 3-29). Assuming daily adult consumption of 2 ℓ of water, it is apparent that the resulting manganese intake of 0.008 mg/day was a very small contribution to the above "Total Diet" estimate of 3.8 mg/day. On the other hand, manganese concentration at the 99th percentile in private wells was 977 µg/ℓ, and therefore it should be recognized

TABLE 3-31

Dietary Intake of Manganese in the U.S.

Group	Average Daily Intake (mg)	Reference
Adults, college women	3.7	North et al., 1960
Adults	2.3-2.4	Schroeder et al., 1966
Adults, males	3.3-5.5	Tipton et al., 1969
Adolescents (15-18 years), males	3.8	U.S. FDA, 1978

TABLE 3-32

Intake of Manganese from Food by Children

Age	Type of Feeding	Daily Intake of Mn in mg	Daily Intake of Mn in mg/kg Body Weight	Reference
1 week	NR	0.0064	0.002	Widdowson, 1969
0-3 months	NR	NR	0.002-0.004	Belz, 1960
1 month	breast milk	0.011	NR	McLeod and Robinson, 1972
1 month	cow's milk	0.024	NR	McLeod and Robinson, 1972
3-4 months	mixed feeding	0.2	NR	McLeod and Robinson, 1972
5-6 months	mixed feeding plus cow's milk	0.4	NR	McLeod and Robinson, 1972
3-5 years	mixed feeding	1.4	0.08	Schlage and Wortberg, 1972
7-9 years	mixed feeding	1.7	NR	Belz, 1960
10-13 years	mixed feeding	2.2	0.06	Schlage and Wortberg, 1972
3 months-8 years	mixed feeding	NR	0.06	Alexander et al., 1974
9-12 years	institutional diet	2.0	NR	Murthy et al., 1971

NR = Not reported

that in extreme instances the drinking water contribution (≈2.0 mg/day) could be substantial. This contribution could be even more substantial for small children consuming 1 ℓ/day (~1 mg Mn/day), when compared with dietary intakes for children (see Table 3-32). In most cases, however, drinking water is not a significant contributor to manganese ingestion when compared to diet.

Clearance of particles from the respiratory tract is an even smaller source. Even assuming 100% deposition and clearance to the gut of inhaled particulate manganese, current ambient exposure (see Table 3-30) results in 0.00026 mg/day (average) or 0.010 mg/day (high). High ambient exposures during the 1960s could have resulted in the ingestion of ~0.15 mg/day.

Therefore, for all practical purposes, ingestion of manganese is determined solely by diet. Estimates for average exposure range from 2.3-5.5 (see Table 3-31), but some variability should be expected due to the widely varying manganese content of foodstuffs.

3.7. SUMMARY OF GENERAL PROPERTIES AND BACKGROUND INFORMATION

3.7.1. Chemical and Physical Properties. Manganese is a ubiquitous element in the earth's crust, in water and in particulate matter in the atmosphere. In the ground state, manganese is a gray-white metal resembling iron, but harder and more brittle. Manganese metal forms numerous alloys with iron, aluminum and other metals (Matricardi and Downing, 1981).

There are numerous valence states for manganese, with the divalent form giving the most stable salts and the tetravalent form giving the most stable oxide. The chlorides, nitrates and sulfates of manganese (II) are highly soluble in water, but the oxides, carbonates and hydroxides are only sparingly soluble. The divalent compounds are stable in acid solution, but are readily oxidized in alkaline conditions. The heptavalent form is found only in oxy-compounds (Reidies, 1981).

3.7.2. Sampling and Analysis. Sampling of manganese in ambient air may be carried out by any of the methods used for collecting atmospheric particulate matter. High-volume samplers with glass fiber filters are widely used by the NASN and by state and local agencies (Thompson, 1979). These samplers usually filter ~2500 m^3 of air in a 24-hour sampling period. High-volume samplers may also be operated with filters composed of organic membrane.

If information on particle size is desired, other types of sampling devices are used. Currently, the type most widely used is the dichotomous sampler, which separately collects fine (<2.5 μm) and coarse (>2.5 μm) particles. The upper size limit of coarse particles may be set at 10, 15 or 20 μm by a size-selective inlet. Particles are usually collected on teflon filters, and sampling time varies from 2-24 hours (Dzubay and Stevens, 1975; U.S. EPA, 1981a).

Sampling of source emissions presents special problems related to gas temperature and flow rate, which affect choice of filtering medium, sampling rate and sampling equipment. Isokinetic or equivalent flow rate into the sampling probe insures representative sampling; membrane filters are not used at high temperatures; and collection of condensate after the filter may also be necessary to prevent complications. Automobile exhaust may be diluted with air to prevent condensation in the sampling train.

Water, soil and food are collected for manganese analysis by the usual techniques insuring representative sampling without contamination. Biological materials such as urine, blood, tissues, hair, etc., are collected and stored so as to prevent contamination by dust; no other special procedures are required when sampling for manganese analysis.

Sample preparation prior to analysis is necessary unless a non-destructive analytical technique is used. Solid samples may be acid digested, with or without prior ashing of organic matter. Extraction of particulate from glass fiber filters is done by sonification in heated, mixed acid without ashing (U.S. EPA, 1983a).

Manganese in an aqueous sample may be preconcentrated by evaporation of the liquid (Boutron and Martin, 1979). If other interfering substances are present, however, a preseparation step may be required. Preseparation may be accomplished by chelation, ion exchange or coprecipitation.

One of the most popular analytical techniques for metals including manganese is atomic absorption spectrophotometry (AAS). Optical emission spectrometry (OES) has been used for analysis of metals from glass fiber filters; inductively coupled argon plasma (ICAP) is the excitation method currently used by EPA with this technique (U.S. EPA, 1983b).

The above are destructive methods. Non-destructive analytical techniques used in multi-elemental analysis are X-ray fluorescence (XRF) and neutron activation analysis (NAA). XRF is the most commonly used method for analysis of particulates on membrane filters.

The detection limits for any technique vary according to sampling method, sample preparation and analytical method. Detection limits for manganese in air are as low as 0.002 $\mu g/m^3$ (Dzubay and Stevens, 1975; U.S. EPA, 1979a).

3.7.3. Production and Use. Very little manganese is mined in this country; some is mined domestically as low-grade ores, but most is imported. Manganese alloys, manganese metal and many compounds of manganese are produced and used in the United States, however. Ferromanganese and silicomanganese are ferroalloys produced by the smelting of manganese ore in an

electric furnace (Maitland and Downing, 1981). Manganese metal is produced by acid leaching of the ore, precipitation of other metals and electrolysis of the solution. Manganese alloys and metal are then used to introduce manganese into steel or nonferrous alloys.

Metallurgy, especially steel making, accounts for ~95% of United States demand for manganese (Reidies, 1981). Ferromanganese production has decreased from 1148×10^3 tons in 1965 to $<120 \times 10^3$ tons in 1982. Silicomanganese production has decreased from 284×10^3 tons in 1968 to $<75 \times 10^3$ tons in 1982. Demand for these products has diminished recently and imports are increasing (Jones, 1982; DeHuff and Jones, 1981; DeHuff, 1961-1980). The remaining 5-6% of manganese demand is for a number of compounds which are important in the chemical industry and in battery manufacture. Manganous oxide (MnO), produced by reduction of manganese dioxide ore, is an important precursor for compounds used as feed additives, fertilizers, colorants and chemical intermediates. Electrolytic MnO_2, also produced from MnO, is used in dry-cell battery manufacture. Potassium permanganate, produced by oxidation of MnO_2 ore, is an important oxidizing agent and catalyst (Reidies, 1981).

Methylcyclopentadienyl manganese tricarbonyl (MMT) has been produced and used in small quantities as a fuel additive since 1958. Major use as an octane improver in unleaded gasoline (at 0.125 g Mn/gal) began in 1974, but was discontinued in 1978 due to adverse effects on hydrocarbon emissions (U.S. EPA, 1977b). MMT continues to be used at ~0.05 g Mn/gal in ~20% of leaded gasoline (Hall, 1983).

3.7.4. Sources of Manganese in the Environment. Manganese is the 12th most abundant element and fifth most abundant metal in the earth's crust. While manganese does not exist free in nature, it is a major constituent in

at least 100 minerals and an accessory element in more than 200 others (Hewett, 1932). Its concentration in various crustal components and soils ranges from near zero to 7000 µg/g; a mean soil content of 560 µg/g has been given (Shacklette et al., 1971). Crustal materials are an important source of atmospheric manganese due to natural and anthropogenic activities (e.g., agriculture, transportation, earth-moving) which suspend dusts and soils. The resulting aerosols consist primarily of coarse particles (>2.5 µm) (Dzubay, 1980; Dzubay et al., 1981).

Manganese is also released to the atmosphere by manufacturing processes. Ferromanganese furnace emissions are composed mainly of fine particulate (<2.5 µm) with a high manganese content (15-25%). Ferroalloy manufacture was the largest manganese emission source in 1968 (U.S. EPA, 1971). Current estimates are not available, but control technology has improved and production volume has diminished. Iron and steel manufacture is also an important manganese source. Manganese content of emitted particles is lower (0.5-8.7%), but overall production volume is greater than for manganese-containing ferroalloys.

Fossil fuel combustion also results in manganese release. The manganese content of coal is 5-80 µg/g (U.S. EPA, 1975). Fly ash is about equal to soil in manganese content (150-1200 µg/g), but contains particles finer in size. This is an important manganese source because of the volume of coal burned each year. Combustion of residual oil is less important because of its lower mangnese content. About 15-30% of manganese combusted in MMT-containing gasoline is emitted from the tailpipe.

The relative importance of emission sources influencing manganese concentration at a given monitoring location can be estimated by chemical mass balance studies. Studies in St. Louis and Denver suggest that crustal

sources are more important in the coarse than in the fine aerosol fraction. Conversely, combustion sources such as refuse incineration and vehicle emissions predominantly affect the fine fraction. In an area of steel manufacturing, the influence of this process was seen in both the fine and coarse fractions (Dzubay, 1980; Dzubay et al., 1981; Alpert and Hopke, 1981; Liu et al., 1982).

Another means of determining the influence of noncrustal sources is to compare the ratio of manganese and aluminum in an aerosol with that in soils. The derived enrichment factor (EF) indicates the magnitude of influences from noncrustal sources. In most areas EF for coarse aerosols is near unity, indicating crustal origin, but EF for the fine fraction is substantially higher, indicating a greater influence from noncrustal sources of emission.

3.7.5. Environmental Fate and Transport Processes. A general overview of man's impact on the geochemical cycling of manganese shows a nearly doubled flux from the land to the atmosphere due to industrial emissions, and a tripled flux from land to oceans, via rivers, due to soil loss from agriculture and deforestation (Garrels et al., 1975).

Atmospheric manganese is present in several forms. Coarse dusts contain manganese as oxides, hydroxides or carbonates at low concentrations ($\leq$1 mg Mn/g). Manganese from smelting or combustion processes is often present in fine particles with high concentrations of manganese as oxides (up to 250 mg/g). Organic manganese usually is not present in detectable concentrations (Coe et al., 1980).

Oxides of manganese are thought to undergo atmospheric reactions with sulfur dicxide or nitrogen dioxide to give the divalent sulfate or nitrate salts (Sullivan, 1969). Manganous sulfate has been shown to catalyze SO_2

transformation to sulfuric acid, but the manganese concentration necessary for a significant catalytic effect has been disputed (Wright et al., 1973; Piver, 1974).

Atmospheric manganese is transported by air currents until dry or wet deposition occurs. In New York City, dry deposition occurred more quickly for manganese than most other metals, because it tended to be present in larger particles. Dry deposition of manganese averaged 300-670 ng/cm^2/month, whereas wet deposition was ~120 ng/cm^2/month (Kleinman et al., 1975; Volchok and Bogen, 1973). Over much of the United States in 1966-1967, wet deposition of manganese ranged from <10-540 ng/cm^2/month (Lazrus et al., 1970). Near a ferromanganese plant in 1964-1965, dry deposition was as high as 19,300 ng/cm^2/month (NAPCA, 1970).

In water or soil, manganese is usually present as the divalent or tetravalent form. Divalent manganese (present as the hexaquo ion) is soluble and relatively stable in neutral or acidic conditions. Chemical oxidation to the insoluble tetravalent form takes place only at a pH above 8 or 9, and chemical reduction of the tetravalent form occurs only at pH <5.5. At intermediate pH, interconversion occurs only by microbial mediation (Alexander, 1977).

Manganese tends to be mobile in oxygen-poor soils and in the groundwater environment (Mitchell, 1971). Upon entering surface water, manganese is oxidized and precipitated, primarily by bacterial action. If the sediments are transported to a reducing environment such as lake bottom, however, microbial reduction can occur, causing re-release of divalent manganese to the water column (Kuznetsov, 1970).

The concentration of manganese in lower organisms is much higher (by a factor of 10^3-10^4) than in the surrounding water. However, the concen-

tration factor is lower ($10-10^2$) as trophic level increases, indicating that the element is metabolically regulated. Thus biomagnification of manganese does not occur (Lentsch et al., 1972).

3.7.6. Environmental Levels and Exposure. Nationwide air sampling has been conducted in some form since 1953 (U.S. DHEW, 1958). Analytical methodology has improved and monitoring stations have changed, complicating any analysis of trends in manganese concentration. However, it is evident that manganese concentrations in ambient air have declined during the period of record. The arithmetic mean manganese concentration of urban samples was 0.11 $\mu g/m^3$ in 1953-1957 (U.S. DHEW, 1958), 0.073 $\mu g/m^3$ in 1966-1967 (McMullen et al., 1970), and decreased to 0.033 $\mu g/m^3$ by 1982 (Barrows, 1983). In 1953-1957, the percentage of urban stations with an annual average of >0.3 $\mu g/m^3$ was ~10%. By 1969 these had dropped to <4%, and since 1972 the number has been <1%.

The highest manganese concentrations, with some observations exceeding 10 $\mu g/m^3$, were seen in the 1960s in areas of ferromanganese manufacture (NAPCA, 1970; U.S. DHEW, 1967). More recent measurements in these areas indicated decreases of at least an order of magnitude had occurred, although definitive studies were not available.

In most cases where comparable data on total suspended particulate (TSP) were available, decreases in TSP also occurred, but were usually smaller in magnitude than those for manganese. This would suggest that the observed reductions in manganese were more than a simple reflection of TSP improvements, indicating specific reductions of manganese emissions.

Techniques for characterizing particle-size distributions for trace metals in ambient aerosol are only recently available. Studies indicate that manganese is associated with both fine (<2.5 μm) and coarse

(>2.5 μm) particles (Bernstein and Rahn, 1979). The manganese concentration in each fraction is highly variable. On the average, ≤16% of manganese in aerosol mass is found in fine particles; however, it is estimated that in some situations the fine fraction could contain as much as 50%.

Manganese concentrations in nonpolluted freshwaters are usually <20 μg/ℓ, but may exceed 1000 μg/ℓ where polluted. The amount of manganese in suspension exceeds the amount in solution, except where acid mine drainage is prevalent (Kopp and Kroner, 1969). Concentrations in groundwater typically are higher than in surface water (Hem, 1970).

Three surveys of United States drinking water supplies have provided data on manganese concentration (Durfor and Becker, 1964; U.S. DHEW, 1970; Greathouse, 1983). Although concentrations ≥1000 μg/ℓ are found in some, notably private, water supplies, ~95% of all supplies contain manganese at <100 μg/ℓ. A median concentration of 4 μg/ℓ for public supplies has been reported (Greathouse, 1983).

Total human exposure to manganese may be estimated from information on levels in air, water and diet. Inhaled particles can be deposited either extrathoracically, in the tracheobronchial region, or in the alveoli. Time required for particle clearance and probability of absorption increases with increasing depth of deposition in the respiratory tract (U.S. EPA, 1982). Deposition of manganese in the alveoli can be calculated from the ambient concentration and the fraction present in fine particles. Thoracic (tracheobronchial plus alveolar) deposition is calculated from estimates of the manganese found in particles ≤15 μm in size. Alveolar deposition of manganese at current ambient levels is estimated as 0.072 μg/day as an average and 6.6 μg/day under high exposure conditions. Estimates of total thoracic deposition are slightly higher; 0.26 μg/day (average) and 10.0 μg/day (high). Alveolar and total thoracic deposition under the high

exposure conditions (10 $\mu g/m^3$) of the 1960s were estimated to be 100 and 152 µg/day, respectively.

Diet is the main source of ingested manganese. Average adult intake has been variously estimated at 2.3-5.5 mg/day. On a body-weight basis, exposure increases from 0.002-0.004 mg/kg/day in infants to 0.06-0.08 mg/kg/day in adults. Drinking water usually comprises only a very small proportion of total ingestion exposure. The median intake level via drinking water is ~0.008 mg/day, but can be as high as ~2.0 mg/day for some water supplies. The ingestion of particles cleared from the respiratory tract is an even smaller source, probably constituting no more than 0.01 mg/day under the highest ambient exposure conditions currently observed.

4. BIOLOGICAL ROLE AND PHARMACOKINETICS

4.1. BIOLOGICAL ROLE OF MANGANESE

Manganese was shown to be essential for growth and reproduction in rats and mice as early as 1931 (Kemmerer et al., 1931; Orent and McCollum, 1931). Later it was demonstrated that manganese prevented a skeletal abnormality in chickens called perosis (Wilgus et al., 1936). Although manganese has been shown to be essential for many species of animals, as yet there are no well-defined occurrences of manganese deficiency in humans (Prasad, 1978).

4.1.1. Biochemical Role. Extensive information is available on the interaction between manganese and proteins (Leach and Lilburn, 1978; Utter, 1976; Prasad, 1978). The relationship between manganese and enzymes can be classified into two categories, metalloenzymes and metal-enzyme complexes (Leach, 1976). The first category of enzymes is very limited, while the enzymes that can be activated are numerous.

Glycosyl transferases are important enzymes in the synthesis of polysaccharides and glycoproteins, and most of these enzymes require manganese for normal activity (Leach, 1971, 1976).

There is substantial experimental evidence that an impairment in glycosaminoglycan metabolism is associated with several symptoms of manganese deficiency (Leach and Lilburn, 1978).

The most extensively studied manganese metalloenzyme is pyruvate carboxylase (Scrutton et al., 1972). Magnesium was found to replace manganese as the bound metal to pyruvate carboxylase isolated from manganese-deficient chicks.

4.1.2. Manganese Deficiency. Manganese deficiency has been demonstrated in mice, rats, rabbits and guinea pigs. The main manifestations of manga-

nese deficiency are those associated with skeletal abnormalities, impaired growth, ataxia of the newborn, and defects in lipid and carbohydrate metabolism.

The skeletal abnormalities of manganese deficiency are described as abnormally fragile bones, with shortening and bowing of the forelegs in mice, rats and rabbits (Amdur et al., 1945; Ellis et al., 1947; Plumlee et al., 1956). This disease is known as perosis in chickens.

Manganese deficiency during pregnancy in rats and guinea pigs produces a congenital defect in the young characterized by ataxia (Hurley, 1968; Everson et al., 1959). This defect is usually associated with loss of equilibrium, increased susceptibility to stimuli, head retraction and tremors.

4.1.3. Manganese Requirements. The minimum daily requirements of manganese for laboratory animals vary with the species and genetic strain of animal, the composition of diet and the criteria of adequacy employed.

Mice, rats and rabbits are unable to grow normally on milk diets containing 0.1-0.2 ppm manganese. The minimum requirment for manganese in the diet of mice has not been established, but diets containing 50 mg/kg manganese were adequate for growth and development of several genetic strains (Hurley and Theriault-Bell, 1974). Although the requirement of manganese for development and growth has not been adequately studied, Holtkamp and Hill (1950) concluded that 50 ppm manganese in diet is optimum for rats.

4.1.4. Summary. Although manganese has been shown to be essential for many species of animals, as yet there are no well-defined occurrences of manganese deficiency in humans. Manganese deficiency has been demonstrated in mice, rats, rabbits and guinea pigs. The main manifestations of manganese deficiency are those associated with skeletal abnormalities, impaired

growth, ataxia of the newborn, and defects in lipid and carbohydrate metabolism. Although the daily requirement of manganese for development and growth has not been adequately studied, it was accepted that diets containing 50 mg/kg manganese are adequate for most of the laboratory animals (NAS, 1973).

4.2. COMPOUND DISPOSITION AND RELEVANT PHARMACOKINETICS

4.2.1. Absorption. The main route of manganese absorption is the gastrointestinal (GI) tract. Absorption through the lung is considered to be an additional route in occupationally exposed workers and in residents living in industrialized areas with higher ambient air concentrations of manganese. Skin absorption of inorganic manganese is not considered to occur to a significant extent.

4.2.1.1. GASTROINTESTINAL ABSORPTION -- Food is generally the main source of manganese. Therefore, the GI tract is the portal of entry of manganese and the absorption from the GI tract is the first step in manganese metabolism. Human and animal studies show that on an average ~3% or less of a single dose of radiolabeled manganese is absorbed from the GI tract irrespective of the amount of stable carrier.

4.2.1.1.1. Human Studies -- Mena et al. (1969) studied manganese absorption in 11 healthy fasted human subjects by administering 100 µCi of $^{54}MnCl_2$ with 200 µg stable $^{55}MnCl_2$ as a carrier. On the basis of whole body counts performed daily for 2 weeks the absorption of ^{54}Mn was calculated to be an average of ~3%. Similar absorption values were obtained in six healthy manganese miners (~3%) and six ex-miners with chronic manganese poisoning (~4%). These values could be an underestimate of the absorption because enterohepatic circulation was not taken into account but the authors considered this to be insignificant.

4.2.1.1.2 Animal Studies -- In an early study using rats Greenberg et al. (1943) estimated that 3-4% of a single oral dose containing 0.1 mg of ^{54}Mn labeled manganese (as chloride) was absorbed from the intestine. This estimation was made on the basis of differences in biliary ^{54}Mn excretion after parenteral and oral administration. Pollack et al. (1965) reported 2.5-3.5% absorption of a single oral dose of ^{54}Mn (as chloride with 5 μmoles stable carrier) in fasted rats. They measured whole-body and gut-free carcass radioactivity 6 hours after administration. The fraction apparently absorbed (i.e., the gut-free carcass retention) could be an underestimate due to the excretion into the intestine. Similarly, Rabar (1976) and Kostial et al. (1978) reported a 0.05% whole-body retention value 6 days after a single oral dose of ^{54}Mn (as chloride-carrier free) in postweaning nonfasted rats. The very low value observed in their experiments can be explained by considerable loss of the absorbed manganese through endogenous fecal excretion within 6 days after administration. It should also be mentioned that higher values obtained in other studies might be due to administration of the isotope to fasted animals.

Little is known about mechanisms involved in manganese absorption. The in vitro experiments performed by Cikrt and Vostal (1969) show that manganese absorption is likely to occur in the small as well as in the large intestine. However, whereas manganese is actively transported in the small intestine, there is only simple diffusion in large intestine. Miller et al. (1972) found that in calves the upper sections of the small intestine absorb far more ^{54}Mn than the lower sections. Manganese excreted into the intestine (biliary excretion being the most important) is known to enter the enterohepatic circulation. Cikrt (1973) showed that manganese excreted in the bile is in a form more easily absorbed than manganese dichloride. He

found that the intraduodenal uptake of biliary excreted manganese was about 35%, whereas only 15% of an equivalent dose of manganese dichloride tered intraduodenally was absorbed.

4.2.1.2. RESPIRATORY ABSORPTION -- There are no quantitative data on sorption rates for inhaled manganese either in humans or in animals. It is assumed that some basic principles considered by the Task Group on Metal Accumulation (TGMA, 1973) can be applied to inhaled metals in general. Only particles small enough (usually several tenths of μm) to reach the alveolar lining are likely to be absorbed directly into the blood. An unspecified fraction of the metal initially deposited in the lung is expected to be removed by mucociliary clearance and consecutively swallowed, thus undergoing gastrointestinal absorption processes.

4.2.1.2.1. Human Studies -- Mena et al. (1969) performed an inhalation study in 21 human subjects exposed for 10 minutes either to a nebulized aqueous solution of $^{54}MnCl_2$ (7 normal controls and 10 exposed working miners) or to a nebulized aqueous suspension of $^{54}Mn_2O_3$ (4 exposed miners). The estimated mean particle size of the droplets delivered through the nebulizer was 1 μm. They found that about 40-70% (average 60%) of the radioactivity initially located in the lung was recovered in the feces collected within 4 days after administration. The fate of manganese oxide was identical to that of the chloride. On the basis of regional radioactivity measurements over different parts of the thoracic and abdominal cavities the authors assumed that the GI tract was a portal of entry for the inhaled manganese. However, as stated by the authors themselves, absorption of the inhaled manganese directly from the lung cannot be excluded. The authors' assumption seems to be highly speculative and experimental data presented are incomplete. Fecal excretion is the main route of manganese

excretion and regional measurements indicating the movement of the isotope through the body do not provide data concerning the direction of movement of the isotope through the intestinal wall (i.e., whether it is being absorbed or excreted).

4.2.1.2.2. Animal Studies -- Pertinent data regarding manganese absorption from the lung in animals could not be located in the available literature.

4.2.2. Distribution and Normal Tissue Levels. Distribution is the term used to describe the uptake of the absorbed manganese by various tissues and organs in pharmacokinetic studies after a single or repeated administration of the radioactive tracer. Such data are almost always obtained in animal studies. Human studies (generally post-mortem analyses of various organs and tissues) reflect the body and organ burden as a consequence of the long-term (lifespan) intake of this essential element.

4.2.2.1. HUMAN STUDIES -- A normal 70 kg man has a total of 12-20 mg manganese in the body (Cotzias, 1958; WHO, 1981). Sumino et al. (1975) found ~8 mg manganese in a group of 30 Japanese cadavers (15 males and 15 females, ~40 years old with an average weight of 55 kg). Muscles contained ~30%, liver ~20%, and the digestive tract ~15% of the total amount. Manganese tissue levels in normal humans from three different studies (Kehoe et al., 1940; Tipton and Cook, 1963; Sumino et al., 1975) are presented in Table 4-1 (WHO, 1981). Although some differences between these studies are obvious (probably due to different analytical techniques used) the highest concentrations were found in liver and pancreas (~1 µg Mn/g wet weight or more). Kidney concentrations were between 0.6 and 0.9 µg/g. Lowest concentrations were found in brain, heart, lung, intestine and gonads (usually between 0.2 and 0.3 µg/g), with extremely low concentrations (<0.10 µg/g) in muscles, bone, fat tissue and spleen.

TABLE 4-1

Manganese in Human Tissues (µg Mn/g wet weight)

Tissue	Kehoe et al., 1940 (emission spectroscopy)	Tipton and Cook, 1963 (emission spectroscopy)	Sumino et al., 1975 (atomic absorption)
Aorta	--	0.11	--
Brain	0.30	0.27	0.25
Fat	--	--	0.07
Heart	0.32	0.23	0.21
Intestine	0.35	--	--
Kidney	0.60	0.90	0.56
Liver	2.05	1.30	1.00
Lung	0.22	0.24	0.22
Muscle	--	0.06	0.09
Ovary	--	0.18	0.19
Pancreas	--	1.10	0.77
Spleen	--	0.11	0.08
Testes	--	0.14	0.20
Trachea	--	0.14	0.20
Rib	--	--	0.06

In spite of appreciable individual variations of manganese concentrations in the liver, there is little variation from one part of the liver to another (Perry et al., 1973). Normal brain concentrations in adults up to 0.6 µg Mn/g wet weight were reported (Fischer and Weigert, 1977). Larsen et al. (1979) studied the topographical distribution of manganese (As and as well) in normal human brain tissue. Manganese was found to be associated with the dry matter of brain tissue and, related to dry weight, equal concentrations were found in white and grey matter. They also found significant differences between 24 different brain regions studied. Mean values were within the range from 0.133-0.449 µg Mn/g wet weight, with highest values observed in the basal ganglia (i.e., nucleus caudatus, globus pallidus and putamen). Similar results with highest concentrations in the basal ganglia were also reported by Smeyers-Verbeke et al. (1976).

The levels in biological fluids (blood and urine particularly) will be discussed in Section 4.2.5.1. concerning their significance in relation to exposure.

4.2.2.2. ANIMAL STUDIES -- Distribution studies in mice (Kato, 1963), rats (Dastur et al., 1969) and monkeys (Dastur et al., 1971) show a high uptake of radioactive manganese by liver, kidneys and endocrine glands, and only minor amounts in brain and bone.

When mice were exposed to MnO_2 by inhalation in concentrations of 5.6 and 8.9 mg/m^3 and particle size of 3 µm for 2 hours daily for 8 and 15 days, respectively, the highest concentrations of manganese were found in the kidney (10.8 and 8.4 mg/kg dry weight), liver (9.0 and 7.1 mg/kg), pancreas (8.4 and 8.2 mg/kg) and brain (5.9 mg/kg) (Mouri, 1973). After intraperitoneal administration of radioactive manganese to rats, the highest concentrations were found in the suprarenal, pituitary, liver and kidney

tissue (Dastur et [illegible] the uptake by glandular structures was also high in monkeys [illegible] peritoneal injection of radioactive manganese (Dastur [illegible].

Schr[illegible] (1981) studied regional distribution of manganese in [illegible]e rats. Two groups of six animals each were given daily i.p. injections of either 3 mg Mn/kg as $MnCl_2 \cdot 4H_2O_2$ or an eq[illegible]volume of 0.9% NaCl for 30 days. Of the thirteen regions examined, the [illegible]st concentrations in normal rats were in hypothalamus, colliculi, olfactory bulbs and midbrain. In treated rats all brain regions showed an increase, the greatest being in the corpus striatum which increased from ~1.7 to 8.8 mg/kg dry weight. On a percentage basis the highest increase was in the corpus callosum, 1300%. This study demonstrated that under these conditions manganese is taken up by striatal, midbrain and thalamic regions at a greater rate than other brain areas. Thus, manganese is selectively concentrated in areas of the extrapyramidal system, which may explain the signs and symptoms of manganism.

In the portal blood most of the manganese may become bound to a α_2-macroglobulin and removed from the blood very efficiently by the liver. A small proportion becomes bound to transferrin, and enters the circulation system to be transported to the tissues. This oxidation step may be performed by ceruloplasmin (Gibbon [illegible]t al., 1976). Within a cell, manganese is sequestered by mitochondria (Maynard and Cotzias, 1955). Tissues rich in mitochondria (liver, kidneys, pancreas) contain higher levels of manganese (Kato, 1963).

The early work of Fore and Morton (1952) showed the constancy of manganese concentrations in different organs for a large number of species.

From their data it is apparent that bones, liver, kidneys and some endocrine glands (pituitary in particular) carry higher manganese concentrations (1.2-3.3 µg Mn/g wet weight) than other organs and tissues (0.18-0.65 µg/g). Brain concentration was 0.40 µg/g and this value is in agreement with human values already discussed.

4.2.3. Excretion. Manganese is almost totally excreted via feces in humans and animals (Newberne, 1973; WHO, 1981). Amounts of manganese excreted via urine, sweat and milk are negligible compared to fecal excretion. Variable excretion is assumed to be the main mechanism in manganese homeostasis (see Section 4.2.5.).

4.2.3.1. HUMAN STUDIES -- Quantitative data concerning manganese excretion in humans are not available (WHO, 1981). Urinary excretion is low indicating that only a small fraction of the absorbed manganese is excreted via that route. Concentrations in urine in unexposed and exposed people will be discussed in Section 4.2.5.1.

4.2.3.2. ANIMAL STUDIES -- Animal studies clearly show that manganese is eliminated from the body mainly via feces. Greenberg and Campbell (1940) reported that 90.7% of a single intraperitoneal dose of 1 mg ^{54}Mn to rats was found in the feces within 3 days after administration. In a subsequent study Greenberg et al. (1943) injected intraperitoneally 0.01 or 0.1 mg of ^{54}Mn to rats and found that 27.1 and 37.3% of the respective dose was collected in the bile within 48 hours. After intravenous administration of 0.6 µg of manganese dichloride in rats 12% of the injected dose was excreted into the bile within 3 hours (Tichy et al., 1973) and 27% within 24 hours (Cikrt, 1972).

Adkins et al. (1980a) studied retention and subsequent clearance of manganese after 2-hour inhalation exposure of Charles River CD-1 mice to 1.8

mg Mn/m^3 as Mn_3O_4 aerosol, with average mass median diameter ~1.4 μm. Seven data points were obtained in 24 hours, each for a group of six mice. The exponential curve fit to the data indicated that ~47, 27 and 14% of the manganese remained 4, 6 and 24 hours after exposure, respectively.

Klaassen (1974) estimated the biliary excretion of manganese in rats, rabbits and dogs after intravenous doses of 0.3, 1.0, 3.0 and 10.0 mg/kg. At the three lower doses the concentration of manganese in bile was 100-200 times higher than in the plasma. Excretion into the bile increased as the dose increased. However, after a dose of 10 mg/kg there was no further increase in excretion of manganese into the bile, and a maximum excretion rate of ≈8.5 μg/min/kg was attained. This indicates that a saturable active transport mechanism may exist for manganese.

Although biliary excretion is particularly important in adjusting the manganese body load, bile is not the exclusive route of manganese excretion. Under ordinary conditions, the bile is the main route of excretion and represents the principal regulatory mechanism, but experiments in animals show conclusively that manganese is also excreted through the intestinal wall (Bertinchamps and Cotzias, 1958; Kato, 1963; Papavasiliou et al., 1966). In rats there is some evidence for the excretion of manganese through the intestinal wall into the duodenum, jejunum and, to a lesser extent, the terminal ileum (Bertinchamps et al., 1966; Cikrt, 1973). In dogs manganese is also excreted to some extent with the pancreatic juice (Burnett et al., 1952). It has been shown that while excretion by the biliary route predominates under normal conditions, excretion by auxiliary GI routes may increase in the presence of biliary obstruction or with overloading of manganese (Bertinchamps et al., 1966; Papavasiliou et al., 1966).

Urinary excretion is low. Klaassen (1974) found that in rats 5 days after intravenous dosing 99% of administered manganese was eliminated in feces and only 0.1% in urine. Biliary obstruction or overloading with manganese did not increase the urinary excretion (Papavasiliou et al., 1966). Moreover, the authors found that animals with rectal obstruction did not excrete measurable quantities of ^{54}Mn via urine within the 5-day observation period. Only after injection of EDTA (ethylene diaminetetra-acetic acid) did urinary excretion become predominant for 24 hours, after which time fecal elimination was resumed (Kosai and Boyle, 1956; Maynard and Fink, 1956).

4.2.4. Biological Half-time.

4.2.4.1. HUMAN STUDIES -- Mahoney and Small (1968) showed that the disappearance rate of labeled manganese from the body of three normal human subjects can be described by a mathematical expression which is the sum of two exponential functions. Each of these processes can be characterized by a "half-time", one of which was 4 days and another which was 39 days. About 70% of the injected manganese was excreted via the slower pathway. In three other subjects with a higher oral intake of manganese, a higher rate of elimination was observed.

Cotzias et al. (1968) studied the tissue clearance of manganese in three groups of humans: healthy subjects, healthy manganese miners and miners removed from manganese exposure but with chronic manganese poisoning. After a single ^{54}Mn injection they found a different total body turnover of the label for the three groups: 37.5, 15 and 28 days, respectively. Regional determination of radioactivity of the liver, head and thigh showed differences among various body areas and differences among groups. The corresponding turnover times for the three groups were: in the liver 25, 13 and 26 days; in the head 54, 37 and 62 days; and in the thigh 57, 39 and 48 days.

4.2.4.2. ANIMAL STUDIES -- Britton and Cotzias (1966) reported a two-component whole body clearance rate for manganese in mice. The half-time of the fast component was 10 days and of the slow component, 50 days. A 10-fold increase in the dietary intake of manganese decreased the half-times of the isotope by about 50%. The effect of dietary manganese levels on the terminal elimination of manganese in mice was studied by Suzuki (1974). The animals received an aqueous solution of manganese chloride in concentrations ranging from 20-2000 mg/ℓ for 30 days before radiomanganese administration. The whole body clearance half-time was estimated at about 6 days in the lowest concentration group. It decreased to 3 days at a manganese concentration of 100 mg/ℓ and to about 1 day in animals receiving 2000 mg/ℓ. The half-time of manganese in the brain was found to be longer than for the whole body. This was also shown for rats (Dastur et al., 1969) and for monkeys (Dastur et al., 1971). In rats the half-time in the whole body was estimated to be 14 days, and in the brain it could not be determined during the observation period of 34 days. In monkeys the half-time in the brain could not be determined after 278 days of observation, while the whole body half-time was estimated to be 95 days.

4.2.5. Homeostasis. As pointed out by Rehnberg et al. (1980), the normal human adult effectively maintains tissue manganese at stable levels despite large variations in manganese intake. Although some workers maintain that this homeostatic mechanism is based on controlled excretion (Britton and Cotzias, 1966; Hughes et al., 1966; Leach, 1976), a critical review of the evidence reveals that manganese homeostasis is regulated at the level of absorption (Abrams et al., 1976a,b) as well as at the level of excretion.

For instance, Lassiter et al. (1974) have provided evidence that the dietary manganese level has a greater effect on manganese absorption than on excretion of endogenous manganese and that both variable excretion and absorption play important roles in manganese homeostasis. In addition, manganese absorption in rats is related to the dietary manganese level (Abrams et al., 1976a,b). In these experiments ^{54}Mn absorption and metabolism were studied in rats fed diets containing 4 ppm (basal), 1000 ppm and 2000 ppm of unlabeled manganese several days prior to a single oral dose of ^{54}Mn. At different time intervals after oral administration, the ^{54}Mn concentration was determined in various tissues. Four hours after administration all tissues from rats fed the basal diet continued to have higher ^{54}Mn concentration than tissues of rats given higher unlabeled manganese in diet. The effect of dietary manganese on tissue ^{54}Mn concentration following oral dosing indicates that variable absorption is an important factor in manganese homeostasis (Abrams et al., 1976b). From 4-24 hours after administration of low and high manganese diets to rats, the relative difference in ^{54}Mn concentration increased in many tissues. This confirms that higher levels of unlabeled dietary manganese accelerates ^{54}Mn turnover after absorption and tissue deposition. Suzuki (1974) reported an intestinal absorption of only 0.5-1.97% of ^{54}Mn in mice prefed diets having levels of MnO_2 ranging from 20-2000 mg/kg. The retention of ^{54}Mn observed in the whole body was inversely proportional to the dietary manganese level.

Absorbed manganese is almost totally excreted via the intestinal wall by several routes, and these routes are interdependent and combined to provide an efficient homeostatic mechanism. Robert (1883) and Cohn (1884) are cited by von Oettingen (1935) as the first to observe that manganese, after large injected doses, was excreted in the feces and only traces appeared in

urine. Subsequent experiments with rats at a lower level (a 1 mg dose) showed that 90% of the intraperitoneally adminstered dose appeared in the feces within 3 days (Greenberg and Campbell, 1940).

Intraperitoneal administration of 0.01 mg manganese to rats resulted in the biliary excretion of 27% of the dose within 48 hours; a dose of 0.1 mg resulted in 37% appearing in the bile (Greenberg et al., 1943). Klaassen (1974) estimated the biliary excretion of manganese in rats, rabbits and dogs after intravenous doses of 0.3, 1.0, 3.0 and 10.0 mg/kg. At the three lower doses, the concentration of manganese in bile was 100-200 times higher than that in the plasma. Excretion into the bile increased as the dose increased. However, after a dose of 10 mg/kg, there was no further increase in excretion of manganese into the bile, and a maximum excretion rate of ~8.5 µg/min/kg was attained. This finding indicates that an apparent maximum transport rate may exist for manganese. Autissier et al. (1982) recently demonstrated that the intraperitoneal administration of the same high dose of manganese (10 mg $MnCl_2$/kg bw) for a period of 4 months resulted in increased brain accumulation of manganese in rats. This manganese treatment gave rise to significant increases in the concentrations of manganese in brain stem (359%), corpus striatum (243%), hypothalamus (138%) and "rest of the brain" (119%).

The efficient operation of the homeostatic mechanism is also reflected by the fact that tissue manganese accumulation differs depending on the routes of administration of this metal. Thus, the results of Autissier et al. (1982) contrast with those of Chan et al. (1981) and Rehnberg et al. (1982). The results from Rehnberg et al. (1982), summarized in Table 4-2, demonstrate that the dose-related increases in manganese levels in brain and

TABLE 4-2

Concentrations of Manganese in Liver, Kidney and Brain[a]
(µg/g wet weight)

Manganese Concentration[b] (ppm)	Liver							Kidney							Brain					
	24	40	60	100 (days)	115	135	224	24	40	60	100 (days)	115	135	224	24	40	60	100 (days)	130	224
50	2.1	2.0	2 1	2.2	2.0	2.8	2.9	0.6	1.3	1.0	0.8	0.6	0.9	1.0	0.5	0.5	0.4	0.4		0.4
400	4.0	2.6	2.6	2.7	2.5	3.7	3.0	0.9	1.3	1.1	1.1	0.7	1.2	1.2	0.8	0.6	0.5	0.4		0.4
1100	6.7	2.8	2.5	2.6	2.4	3.4	3.4	1.5	1.4	1.2	1.0	0.8	1.2	1.2	1.4	0.7	0.6	0.4		0.4
3550	17.0	4.6	3.5	3.3	3.1	4.7	4.0	2.6	2.0	1.2	1.0	0.9	1.5	1.2	2.7	1.1	0.7	0.5		0.5

[a]Adapted from Kehnberg et al., 1982

[b]Mn_3O_4 in diet

kidney resulting from chronic feeding with manganese varying from 50-3550 ppm were not quite as high as one might anticipate. Chan et al. (1981) only observed a small increase (31%) in brain manganese concentration in rats exposed to 278 ppm Mn as $MnCl_2$ in the drinking water for over 2 years. Liver values were up 45%.

Klaassen (1974) demonstrated that manganese is excreted into the bile against a concentration gradient. On the other hand, Tichy and Cikrt (1972) suggested that manganese may be transferred from plasma into the bile by passive transfer followed by a nonenzymatic complex formation in the bile. However, in contrast to bile, plasma and liver contain ligands with higher affinity for manganese (Klaassen, 1974). Thus, the transfer of manganese from plasma to bile may be mediated by an active mechanism.

Although normally biliary excretion is particularly important in regulating the body burden of manganese, this route of excretion is by no means exclusive. This is because experiments in animals and humans conclusively demonstrate that manganese is also excreted through the intestinal wall (Bertinchamps and Cotzias, 1958; Kato, 1963; Papavasiliou et al., 1966; Wassermann and Mihail, 1964). For instance, there is some indication of manganese excretion through the rat intestinal wall into the duodenum, the jejunum and, to a lesser extent, the terminal ileum (Bertinchamps et al., 1966; Cikrt, 1972). Both of these routes of excretion contribute significantly toward the homeostasis of tissue contents of manganese. In addition, manganese is also excreted to some extent with the pancreatic juice (Burnett et al., 1952); manganese excretion by auxiliary GI routes may increase in the presence of biliary obstruction or with manganese overloading (Bertinchamps et al., 1966; Papavasiliou et al., 1966).

4 2.5.1. LEVELS IN BIOLOGICAL FLUIDS AND BIOLOGICAL INDICATORS OF EXPOSURE -- Concentrations of the metal in biological media have been studied as indicators of exposure. The correlations between the manganese contents in blood and urine and the findings of neurological symptoms and signs have also been examined. Manganese concentrations in body fluids have not, however, proven to be reliable indicators of exposure.

The mean concentration of manganese in the urine of nonexposed people is usually estimated to be between 1 and 8 µg/ℓ, but values up to 21 µg/ℓ have been reported (Horiuchi et al., 1967; Tichy et al., 1971). Tanaka and Lieben (1969) have shown that a rough correlation may exist between mean urinary levels and average occupational air concentrations of manganese, but in individual cases the correlation is poor. Horiuchi et al. (1967) and Chandra et al. (1981) have also associated increased mean urine manganese levels with increased levels of manganese in the air.

Recent studies that used neutron activation and electrothermal atomic absorption analytic procedures have shown that the average normal concentration of manganese in whole blood is 0.7-1.2 µg/100 mℓ, and that manganese concentration is much higher in the erythrocytes than in plasma or serum (Cotzias et al., 1966; Cotzias and Papavasiliou, 1962; Papavasiliou and Cotzias, 1961; Papavasiliou et al., 1966; Muzzarelli and Rocchetti, 1975; Buchet et al., 1976; Tsalev et al., 1977; Zielhuis et al., 1978; Diehy et al., 1966). The average manganese blood level in exposed workers seems to be of the same order as that in nonexposed persons, but some observations indicate that heavy exposures to manganese may increase the level of manganese in the blood. Tsalev et al. (1977) found that workers exposed to ≈1 mg of manganese dust/m^3 of air, for a period of 1-10 years, had blood

levels of manganese averaging 11-16 µg/ℓ compared to a mean level of 10 µg/ℓ in nonexposed persons. Variations in plasma manganese concentrations in women may be associated with hormonal changes (Hagenfeldt et al., 1973). Slight seasonal (Horiuchi et al., 1967) and diurnal (Sabadas, 1969) variations in blood manganese concentrations (lower during summer, autumn and at night) have also been reported. Manganese concentrations did not differ among adult age groups (Horiuchi et al., 1967) and several studies indicate that there is no difference in the concentration of manganese in the blood of men and women (Horiuchi et al., 1967; Zhernakova, 1967; Mahoney et al., 1969; Versieck et al., 1974).

There is only one study indicating a correlation between the manganese blood and urine levels and the findings of neurological symptoms and signs (Horiuchi et al., 1970). Using the results of medical examinations performed in three groups of workers employed in crushing manganese ore, manufacturing dry-cell batteries and electrodes, Horiguchi et al. (1966), found a tendency toward anemia as determined from the specific gravity of whole blood, a decrease in white blood cell count, and an increase in neurological findings. A significant association was reported ($p<0.05$) between the urine manganese level and the neurological findings for all the groups taken together. In the manganese ore-crushing workers (the group with the highest mean exposure), a significant association was determined between manganese levels in the whole blood and urine and in the neurological findings. Other investigators reported that the manganese of blood is unrelated to clinical neurological findings (Rodier, 1955; Penalver, 1955).

The determination of manganese in feces has been recommended as a group test for the evaluation of the level of occupational exposure to manganese (Jindrichova, 1969). Manganese content in hair is normally below 4 mg/kg

(Eads and Lamb3in, 1973). There is as yet no consensus on other biological materials which could be used to monitor manganese exposure. Chandra et al. (1974) suggested using serum calcium to diagnose early exposure, and subsequently found an increase in calcium in exposed welders (Chandra et al., 1981).

4.2.6. Summary. On the basis of human (Mena et al., 1969) and animal data (Pollack et al., 1965; Kostial et al., 1978) it is generally accepted that ~3% or less of a single oral dose of manganese is absorbed from the GI tract under normal conditions. There are neither human nor animal data suggesting the rate of absorption of manganese through the lung.

Manganese is widely distributed within the body in constant concentrations which are characteristic for individual tissues and almost independent of the species (Fore and Morton, 1952). The concentration of manganese present in individual tissues, particularly in the blood, remains remarkably constant in spite of some rapid phases in manganese transport. The average normal level of manganese in whole blood of humans is 7-12 µg/ℓ, while the manganese levels in serum are normally distributed around a mean value of 0.5-0.5 µg/ℓ (Versieck and Cornelis, 1980). The highest values of manganese in humans are found in liver, kidney and endocrine glands which do not exceed 2 µg/g wet weight of tissue. Manganese penetrates the blood-brain and placental barrier. Animal data indicate a higher manganese accumulation in suckling animals, especially in the brain (Kostial et al., 1978).

Fecal excretion is the most important way of manganese elimination from the body. Biliary excretion is predominant under normal conditions (Klaassen, 1974) although excretion via pancreatic juice and intestinal wall are considered to be important in conditions of biliary obstruction or manganese overload (Papavasiliou et al., 1966). In humans and in animals urinary excretion is low (Klaassen, 1974).

The total body clearance of manganese in humans can be described by a curve which is the sum of at least two exponential functions with half-times of 4 and 40 days, respectively. However, the physical significances of the estimated half-times cannot be obtained from this data.

Manganese metabolism is rigorously controlled by homeostatic mechanisms. The homeostatic control is primarily exerted at the level of excretion; however, the site of GI absorption may also be an important control point. The absorption, retention and excretion of manganese are closely linked and interrelated and respond very efficiently to an increase in manganese concentration. The GI absorption depends not only on the amount ingested and tissue levels of manganese, but also on manganese bioavailability and interaction with other metals. The way tissue concentrations influence the excretory mechanism is still unknown. Bile is the most important route of excretion.

4.3. SYNERGISTIC/ANTAGONISTIC FACTORS

The way in which the body normally handles manganese is affected by the age of the individual and by the status of other metals in the body. The effect of iron stores has been the subject of several studies.

4.3.1. Interaction with Metals.

4.3.1.1. HUMAN STUDIES -- Thomson et al. (1971) studied the intestinal transport system for manganese and iron in subjects with three different levels of iron stores: those with normal iron stores, patients with iron deficiency, and patients with endogenous iron overload. Administration of manganese by a duodenal sonde in these patients showed that the rate of absorption was increased in iron-deficient patients and that this enhanced absorption could be inhibited by addition of iron.

Recent balance studies performed in humans showed no effect of dietary calcium on manganese balance. Price and Bunce (1972) studied the influence of calcium intake (300-1300 mg daily) on the balance of several essential elements including manganese in 7- to 9-year-old girls. The researchers concluded that the calcium intake in this study had no effect on manganese balances.

4.3.1.2. ANIMAL STUDIES -- Considerable investigation has been made of the relationship between iron and manganese. The addition of manganese to diets of several species of animals depleted of iron resulted in depressed hemoglobin levels. Wilgus and Patton (1939) reported that addition of ferric citrate to the diet of chickens accentuated the severity of perosis. Matrone et al. (1959) found that excessive manganese in the diet (2000 ppm) depressed hemoglobin formation in both rabbits (~88% of control levels) and baby pigs (~50% of control levels). The minimal level of manganese in the diet that interfered with hemoglobin formation was estimated to be 50 and 125 ppm, respectively.

The interaction of iron and manganese metabolism in rats was also studied by Diez-Ewald et al. (1968). When iron absorption was increased in iron deficiency, manganese absorption was also increased. Decreased iron absorption in iron loaded animals was associated with decreased manganese absorption. The body compensated for changes in manganese absorption by increasing manganese excretion in iron-deficient states and decreasing manganese excretion in iron loaded states.

Kostial et al. (1980) found that increasing the iron content of milk decreased the whole body retention of orally administered ^{54}Mn by a factor of 10 in rats fed milk with or without 100 ppm iron additive. Thomson and Valberg (1972) and Thomson et al. (1971) studied the interrelationship of

the intestinal transport system for manganese and iron by using the technique of open-ended duodenal loops in control and iron-deficient rats. They found that manganese competes with iron and cobalt in the process of uptake from the lumen into the mucosal cells and in the transfer across the mucosa into the body.

Manganese interaction with other elements such as Zn, Cu, Cr, Co, Cd, Ni, In, Rh and Se have also been described (Doyle and Pfander, 1975; Jacobs et al., 1978; Burch et al., 1975; Schroeder et al., 1974; Schroeder and Mason, 1976). Most of these interactions occurred at the level of gastrointestinal absorption and under specific conditions, i.e. the concentrations of other nonessential elements exceeded the normal levels by several orders of magnitude. These interactions are not discussed because of their limited relevance to evaluating the human health risk of manganese inhalation.

4.3.2. Effect of Age.

4.3.2.1. HUMAN STUDIES -- Several studies indicate that age is an important factor in manganese absorption and retention starting with the fetal stage through adult life. Studies by Schroeder et al. (1966) and Widdowson et al. (1972) confirm that human placental transfer of manganese takes place.

In contrast to some other essential metals, manganese levels in the fetus and newborn are similar to adult levels (Fischer and Weigert, 1977; Casey and Robinson, 1978). The exception seems to be bone, where fetal concentration is higher than in the adult (Casey and Robinson, 1978; Sumino et al., 1975). In fetal liver and kidney, concentrations of ~0.94 and 0.45 mg/kg have been found (Casey and Robinson, 1978). In the newborn, corresponding values were 0.52 and 0.48 mg/kg, respectively (Fischer and

Weigert, 1977). Widdowson et al. (1972) reported that there was no consistent change in the liver with age in 30 fetuses from 20 weeks of gestation to full term but that generally manganese concentrations in full-term livers were 7-9% higher than concentrations in adult livers.

In contrast to many other trace metals, manganese does not accumulate significantly in the lungs with age (Newberne, 1973). In lungs of both the adult and the fetus, average concentrations of ~0.2 mg/kg manganese have been reported (Schroeder et al., 1966; Sumino et al., 1975; Casey and Robinson, 1978).

Data reported by Fischer and Weigert (1977) indicate a tendency to decreasing renal manganese levels above age 50. Data reported by Schroeder et al. (1966) show a difference between subjects 20-49 and 50-59 years of age. Anke and Schneider (1974) report a slightly higher mean concentration of manganese in females than in males.

Several studies indicate that manganese penetrates the placental barrier and that manganese is more uniformly distributed in fetal than in adult tissues (Koshida et al., 1963; Onoda et al., 1978). Koshida found that fetal tissue concentrations of manganese except kidney and liver were higher than concentrations of comparable adult tissue. Onoda et al. (1978) found, however, that all measured fetal tissues (including kidney and liver) had higher concentrations of manganese. At a later embryonic stage manganese accumulation takes place parallel to ossification (Koshida et al., 1963).

4.3.2.2. **ANIMAL STUDIES** -- Rabar (1976) and Kostial et al. (1978) observed much higher manganese absorption in artificially fed suckling rats than in adult animals. Absorption of ^{54}Mn in older animals fed on milk diet was also higher (6.4%) than in rats on control diet (0.05%) but never as high as in newborn rats. These results indicate that both age and milk

diet cause very high absorption (40%) of manganese in the immature. The addition of manganese to milk decreased the percentage of absorption of ^{54}Mn in both suckling and adult rats, indicating the existence of a homeostatic control mechanism in neonates which, however, seemed to be less effective in newborns.

Miller et al. (1975) found that neonatal mice did not excrete manganese for the first 17-18 days of life, although absorption as well as distribution, tissue accumulation and mitochondrial accumulation of elemental manganese was vigorous. This suggested an initially avid accumulation of manganese that was supplied in trace amounts in the mouse milk (54 ng/mℓ). The presence of high absorption coupled with the absence of excretion resulted in a marked rise of tissue manganese in the neonates from an exceedingly low to a very high level.

The tissue accumulation in the brain was particularly impressive as the brain can be susceptible to both manganese poisoning and deficiency. Miller and Cotzias (1977) noticed an absence of manganese excretion during the first 18 days of life in neonatal rats and kittens. However, when lactating mothers were given drinking water with concentrations of manganese ranging from 40-40,000 mg/ℓ, th[illegible]tation barrier appeared to give adequate protection to the young[illegible]e level exceeded 280 mg/ℓ, newborn animals initiated excretion before the 16th day of life. The neonates showed a greater accumulation in the brain than their mothers, whereas the increase in liver concentrations was proportional to the concentrations found in the liver of their mothers.

Silbergeld (1982) reports that older rats (24-32 months) had greater striatal dopamine levels than younger rats (2-3 months) when manganese acetate was added to the drinking water. Thus, the ageing brain is suggested as an organ of special sensitivity.

Kostial et al. (1978) found a difference between ^{54}Mn distribution in the newborn as compared to older rats. Most striking was the 34 times higher manganese uptake in the brain of 6-day-old sucklings as compared to adult females. These findings suggest that the neonatal brain may be at a higher risk of reaching abnormal concentrations than are other tissues. Rehnberg et al. (1980) found that the tissue distribution of manganese oxide in preweanling rats after oral exposure was: liver > brain ≒ kidney > testes at 18-21 days of age. Subsequent studies of longer duration (Rehnberg et al., 1981, 1982) gave similar results and indicated the dietary iron deficiency caused a greater accumulation of tissue manganese. These authors concluded that maximum manganese oral absorption and retention in rats occurs during the preweanling period. Cahill et al. (1980) found that preweanling rats retained up to 12 times more manganese when the chloride was ingested compared to the oxide.

4.3.3. Summary. It is generally accepted that under normal conditions 3-4% of orally ingested manganese is absorbed in man (Mena et al., 1969) and other mammalian species (Pollack et al., 1965). Gastrointestinal absorption of manganese and iron may be competitive (Mena et al., 1969; Kostial et al., 1980). This interaction has a limited relevance to human risk assessment under normal conditions. However, it does lead to the hypothesis that iron-deficient individuals may be more sensitive to manganese than the normal individual.

Evidence is accumulating that during mammalian development manganese absorption and retention are markedly increased (Kostial et al., 1978) giving rise to increased tissue accumulation of manganese (Cahill et al., 1980; Chan et al., 1983).

Manganese does penetrate the blood-brain barrier and the placental barrier. Studies in animals indicate a higher manganese concentration in suckling animals, especially in the brain (Kostial et al., 1978).

5. TOXIC EFFECTS AFTER ACUTE EXPOSURE

5.1. ANIMAL STUDIES

The average median lethal doses (LD_{50}) observed in different animal experiments are presented in Table 5-1. These data indicate some variance among LD_{50} doses reported by different researchers, which may be attributed to the specific experimental design used (i.e., route of exposure, chemical form, animal species, or even age of animals). Generally, oral doses are much less toxic than parenteral doses. The average LD_{50} values range from 400-830 mg Mn/kg for oral administration of soluble manganese compounds and from 38-64 mg Mn/kg for parenteral injection. These data also show that the toxicity of manganese varies with the chemical form administered to animals. It has been suggested that cationic manganese forms are more toxic than the anionic forms and that the bivalent cation is ~3 times more toxic than a trivalent cation (U.S. EPA, 1975). Although the permanganate anions are strong oxidizing agents which show some caustic action, they are relatively less toxic than the cationic forms. Obviously, insoluble manganese oxide is less toxic than several of the soluble compounds (Holbrook et al., 1975). However, as seen from Table 5-1, it is very difficult to conclude from the data how the type of manganese ion influences its toxicity. Comparative intraperitoneal toxicity studies have shown that manganese is less toxic than many other metals (Franz, 1962; Bienvenu et al., 1963).

Kostial et al. (1978) found that age plays an important role in the pharmacokinetics and toxicity of heavy metals. The highest oral toxicity of manganese was found in the oldest and youngest groups of rats, as indicated in Table 5-2. In 3- and 6-week-old rats a sharp decrease in toxicity was noted when compared to sucklings; LD_{50} values were increased by a factor

TABLE 5-1

Acute LD_{50} Values for Manganese Compounds

Compound	Valence	Exposure Route	Animal	LD_{50} (mg Mn/kg)	Reference
Manganese chloride	2+	oral	mouse	450	Sigan and Vitvickaja, 1971
		oral	rat	425	Sigan and Vitvickaja, 1971
		oral	guinea pig	400	Sigan and Vitvickaja, 1971
		oral	rat	410	Holbrook et al., 1975
		oral	rat	475	Kostial et al., 1978
Manganese acetate	2+	oral	rat	836	Smyth et al., 1969
Potassium permanganate	7+	oral	mouse	750	Sigan and Vitvickaja, 1971
		oral	rat	750	Sigan and Vitvickaja, 1971
		oral	guinea pig	810	Sigan and Vitvickaja, 1971
Manganese dioxide	4+	oral	rat	7400	Holbrook et al., 1975
Manganese sulfate	2+	i.p.	mouse	44	Blenvenu et al., 1963
		i.p.	mouse	64	Yamamoto and Suzuki, 1969
Manganese nitrate	2+	i.p.	mouse	56	Yamamoto and Suzuki, 1969
Manganese chloride	2+	i.p.	mouse	53	Franz, 1962
		i.p.	rat	38	Holbrook et al., 1975

TABLE 5-2

Influence of Age on Manganese Toxicity in Rats:
LD_{50} Values 8 Days after a Single Oral
Administration of $MnCl_2$*

	Average and Range of LD_{50} (mg/kg) Values	
Age in Weeks	$MnCl_2 \cdot 4H_2O$	Actual Mn Dose
2	804 (735-897)	223 (204-249)
3	1860 (1655-2009)	516 (459-557)
6	1712 (1553-1887)	475 (431-524)
18	850 (775-957)	236 (215-265)
54	619 (564-702)	171 (156-194)

*Source: Kostial et al., 1978

of 2-3. In adult rats toxicity increased again and reached values in the oldest animals similar to those of suckling rats. The researchers suggested that older rats might be more susceptible to metal toxicity due to a general decrease in adaptive responsiveness, which is characteristic of the aging process. It is difficult to evaluate the contribution of aging because the animals were only about 1 year old. Increased toxicity in suckling rats might occur as a result of higher intestinal manganese absorption and higher body retention, observed earlier by some authors (see Chapter 4).

5.2. HUMAN STUDIES

Acute poisoning by manganese is very rare. It may occur in exceptional circumstances such as accidental or intentional ingestion of large amounts of manganese compounds. Dagli et al. (1973) described a case where extensive damage to the distal stomach, resulting in pyloric stenosis, occurred 2 hours after ingestion of potassium permanganate (10 tablets of 300 mg each). Mahomedy et al. (1975) reported two cases of lethal methemoglobinemia induced by potassium permanganate prescribed by African witch doctors.

Manganese, along with other metals such as zinc, copper, magnesium, aluminum, antimony, iron, nickel, selenium, silver and tin, has been reported to cause metal fume fever in humans. Metal fume fever is an acute effect of occupational exposure to freshly formed metal oxide fumes of respirable particle size. The symptoms are similar to those of influenza consisting of fever, chills, sweating, nausea, and cough. The syndrome begins 4-12 hours after sufficient exposure and usually lasts for 24 hours without causing any permanent damage. The mechanisms are not fully understood (Piscator, 1976).